10/017,216

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=> d his

     (FILE 'HOME' ENTERED AT 14:53:07 ON 03 AUG 2004)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 14:56:53 ON 03 AUG 2004
L1         14352 S MYOTONIC (A) DYSTROPHY
L2       1222659 S KINASE?
L3           999 S L1(4W)L2
L4           119 S HUMAN(A)L3
L5       6636677 S CLON? OR EXPRESS? OR RECOMBINANT
L6             0 S HUMAN(A) MDPK
L7            15 S  "MDPK"
L8           133 S L4 OR L7
L9            86 S L5 AND L8
L10           37 DUP REM L9 (49 DUPLICATES REMOVED)
L11           44 S "13245"
L12            3 S L2 AND L11
L13            2 DUP REM L12 (1 DUPLICATE REMOVED)
                 E KAPELLER-LIBERMANN R/AU
                 E KAPELLER R/AU
                 E KAPELLERLIBERMANN R/AU
                 E KAPELLER(W)LIBERMANN R/AU
                 E KAPELLERL R/AU
                 E KAPELLER L R/AU
L14          191 S E5-E10
L15            2 S L8 AND L14
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 NEWS  3  May 12  EXTEND option available in structure searching
 NEWS  4  May 12  Polymer links for the POLYLINK command completed in REGISTRY
 NEWS  5  May 27  New UPM (Update Code Maximum) field for more efficient patent
                  SDIs in CAplus
 NEWS  6  May 27  CAplus super roles and document types searchable in REGISTRY
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                  and WATER from CSA now available on STN(R)
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                  with the 228th ACS National Meeting
 NEWS 11  AUG 02  IFIPAT/IFIUDB/IFICDB reloaded with new search and display
                  fields
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FULL ESTIMATED COST                                    1.26       1.26

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FILE 'LIFESCI' ENTERED AT 14:56:53 ON 03 AUG 2004
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=> s Myotonic (a) Dystrophy
L1        14352 MYOTONIC (A) DYSTROPHY

=> s kinase?
L2      1222659 KINASE?

=> s l1(4w)l2
L3          999 L1(4W) L2

=> s human(a)l3
L4          119 HUMAN(A) L3

=> s clon? or express? or recombinant
   5 FILES SEARCHED...
L5      6636677 CLON? OR EXPRESS? OR RECOMBINANT

=> s human(a) MDPK
L6            0 HUMAN(A) MDPK

=> s  "MDPK"
L7           15 "MDPK"

=> s l4 or l7
L8          133 L4 OR L7

=> s l5 and l8
L9           86 L5 AND L8

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10          37 DUP REM L9 (49 DUPLICATES REMOVED)

=> d 1-37 ibib ab
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L10 ANSWER 1 OF 37 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-16673 BIOTECHDS
TITLE: **Human myotonic dystrophy** protein **kinase** 61.27-polypeptide, encoding polynucleotide, antagonist and **recombinant** production, useful for treating senile dementia and embryo developmental disorders;
involving vector-mediated gene transfer and **expression** in host cell for use in senile dementia and embryo developmental disorder therapy
AUTHOR: MAO Y; XIE Y
PATENT ASSIGNEE: BIOWINDOW GENE DEV INC SHANGHAI
PATENT INFO: CN 1393552 29 Jan 2003
APPLICATION INFO: CN 2001-113166 29 Jun 2001
PRIORITY INFO: CN 2001-113166 29 Jun 2001; CN 2001-113166 29 Jun 2001
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
OTHER SOURCE: WPI: 2003-422183 [40]
AB DERWENT ABSTRACT:
NOVELTY - **Human myotonic dystrophy** protein **kinase** 61.27-polypeptide, encoding polynucleotide, antagonist and **recombinant** production, are new.
USE - The polypeptide is useful for treating senile dementia and embryo developmental disorders.

L10 ANSWER 2 OF 37 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:141446 BIOSIS
DOCUMENT NUMBER: PREV200300141446
TITLE: Changes in myotonic dystrophy protein kinase levels and muscle development in congenital myotonic dystrophy.
AUTHOR(S): Furling, Denis; Lam, Le Thanh; Agbulut, Onnik; Butler-Browne, Gillian S.; Morris, Glenn E. [Reprint Author]
CORPORATE SOURCE: Biochemistry Group, North East Wales Institute, Mold Road, Wrexham, LL11 2AW, UK
morrisge@newi.ac.uk
SOURCE: American Journal of Pathology, (March 2003) Vol. 162, No. 3, pp. 1001-1009. print.
ISSN: 0002-9440 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Mar 2003
Last Updated on STN: 19 Mar 2003
AB Myotonic dystrophy (DM1) is caused by the expansion of a CTG repeat in the noncoding region of a protein kinase, DMPK, **expressed** in skeletal and cardiac muscles. The aim of the present study was to determine the effects of very large CTG expansions on DMPK **expression** and skeletal muscle development. In fetuses suffering from the severe congenital form of DM1 with large CTG expansions (1800 to 3700 repeats), the skeletal muscle level of DMPK was reduced to 57% of control levels and a similar reduction was observed in cultured DM1 muscle cells relative to control cultures. These results are consistent with greatly reduced DMPK **expression** from the mutant allele and normal **expression** from the unaffected allele in this autosomal dominant disorder. In normal fetuses, DMPK protein levels increased dramatically between 9 and 16 weeks and remained high throughout the remaining gestation period. DM1 fetuses showed impaired skeletal muscle development, characterized by a persistence of embryonic and fetal myosin heavy chains and almost total absence of slow myosin heavy chains at the end of gestation. DMPK **expression**, however, was similar in both fast and slow fibers from normal adult muscle. The reduced DMPK and the delayed slow fiber maturation in congenital DM1 may be two separate consequences of nuclear retention of DMPK RNA transcripts with expanded CUG repeats.

L10 ANSWER 3 OF 37 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2003377329 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12912889
TITLE: Environmental suppression of Neurospora crassa cot-1 hyperbranching: a link between COT1 kinase and stress sensing.
AUTHOR: Gorovits Rena; Yarden Oded
CORPORATE SOURCE: Department of Plant Pathology and Microbiology. The Otto Warburg Center for Agricultural Biotechnology, Faculty of Agricultural, Food and Environmental Quality Sciences, The Hebrew University of Jerusalem, Rehovot 76100, Israel.
SOURCE: Eukaryotic cell, (2003 Aug) 2 (4) 699-707.
Journal code: 101130731. ISSN: 1535-9778.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 20030813
Last Updated on STN: 20040413
Entered Medline: 20040412

AB cot-1 mutants belong to a class of Neurospora crassa colonial temperature-sensitive (cot) mutants that exhibit abnormal polar extension and branching patterns when grown at restrictive temperatures. cot-1 encodes a Ser/Thr protein kinase that is structurally related to the **human myotonic dystrophy kinase** which, when impaired, confers a disease that involves changes in cytoarchitecture and ion homeostasis. When grown under restrictive conditions, cot-1 cultures exhibited enhanced medium acidification rates, increased relative abundance of sodium, and increased intracellular glycerol content, indicating an ion homeostasis defect in a hyperbranching mutant. The application of ion transport blockers led to only mild suppression of the cot-1 phenotype. The presence of increased medium NaCl or sorbitol, H(2)O(2), or ethanol levels significantly suppressed the cot-1 phenotype, restored ion homeostasis, and was accompanied by reduced levels of cyclic AMP-dependent protein kinase (PKA) activity. The cot-1 phenotype could also be partially suppressed by direct inhibition of PKA with KT-5720. A reduced availability of fermentable carbon sources also had a suppressive effect on the cot-1 phenotype. In contrast to the effect of extragenic ropy suppressors of cot-1, environmental stress-related suppression of cot-1 did not change COT1 polypeptide **expression** patterns in the mutant. We suggest that COT1 function is linked to environmental stress response signaling and that altering PKA activity bypasses the requirement for fully functional COT1.

L10 ANSWER 4 OF 37 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003530022 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 14607980
TITLE: Overexpression of **human myotonic dystrophy** protein **kinase** in Schizosaccharomyces pombe induces an abnormal polarized and swollen cell morphology.
AUTHOR: Sasagawa Noboru; Kino Yoshihiro; Takeshita Yuya; Oma Yoko; Ishiura Shoichi
CORPORATE SOURCE: Department of Life Sciences, Graduate School of Arts and Sciences, University of Tokyo, Tokyo 153-8902.. csasa@mail.ecc.u-tokyo.ac.jp
SOURCE: Journal of biochemistry, (2003 Oct) 134 (4) 537-42.
Journal code: 0376600. ISSN: 0021-924X.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals

ENTRY DATE: Entered STN: 20031111
Last Updated on STN: 20040117

AB We **expressed human myotonic dystrophy** protein **kinase** (DMPK) in the fission yeast Schizosaccharomyces pombe, in which the overexpression of human DMPK affects cell growth and cell shape. The human DMPK protein has a leucine-rich domain at the N-terminus, a serine/threonine kinase domain in the middle, and a hydrophobic region at the C-terminus. C-Terminus-deleted DMPK produced a middle-swollen phenotype (lemon-like shape), indicating an abnormality in cell division. On the other hand, when both the kinase domain and C-terminus were present, the **expression** of DMPK resulted in polarized cell growth and multinucleated/branched cells. The lemon-like phenotype seen with the C-terminus-deleted DMPK disappeared when the ATP binding site of DMPK was disrupted by replacing the lysine at amino acid 100 with arginine (K100R mutant). However, polarized and/or multinucleated cells lacking the DMPK N-terminus were not rescued by the K100R mutation. Therefore, we conclude that the N-terminus of DMPK plays an important role in DMPK kinase activity, and that the C-terminus of DMPK determines the intracellular localization of the protein.

L10 ANSWER 5 OF 37 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2003:196119 SCISEARCH
THE GENUINE ARTICLE: 647ZT
TITLE: Genomic organization of **human myotonic dystrophy kinase**-related Cdc42-binding **kinase** alpha reveals multiple alternative splicing and functional diversity
AUTHOR: Tan I; Cheong A; Lim L; Leung T (Reprint)
CORPORATE SOURCE: Glaxo, IMCB Grp, Inst Mol & Cell Biol, 30 Med Dr, Singapore 117609, Singapore (Reprint); Glaxo, IMCB Grp, Inst Mol & Cell Biol, Singapore 117609, Singapore; UCL, Neurol Inst, Dept Mol Pathogenesis, London WC1N 1PJ, England
COUNTRY OF AUTHOR: Singapore; England
SOURCE: GENE, (30 JAN 2003) Vol. 304, pp. 107-115.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0378-1119.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 36
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Myotonic dystrophy kinase-related Cdc42-binding kinase alpha (MRCKalpha) is a Cdc42/Rac interactive binding-containing serine/threonine kinase with multiple functional domains. Its roles in the regulation of peripheral actin reorganization in HeLa cells and NGF-induced neurite outgrowth in PC12 cells have been documented. Here we report the characterization of the genomic structure and alternative splicing of the human counterpart. Human MRCKalpha gene is located on chromosome 1q42.1, spanning a genomic region of 250-300 kb and is composed of 41 exons. Four exons in the internal variable region and six in the 3' end were found to undergo extensive alternative splicing, giving rise to 96 possible transcripts of different combinations. The region of the internal splice site that defines a variable region in between two functional domains of opposite regulatory effects on MRCKalpha catalytic activity, and the 3' end splice site that generates variants with differential GTPase binding activity suggest a role for these alternative splicing events in MRCKa regulation. (C) 2002 Elsevier Science B.V. All rights reserved.

L10 ANSWER 6 OF 37 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
DUPLICATE 3
ACCESSION NUMBER: 2002-17868 BIOTECHDS
TITLE: **Human myotonic dystrophy** type

protein **kinase** polypeptide and polynucleotide useful for prognosticating, diagnosing, preventing or inhibiting tumorigenesis, tumor growth, tumor metastasis and viral infection;
vector-mediated **recombinant** protein gene transfer and **expression** in host cell for use in drug screening and gene therapy

AUTHOR: KAPELLER-LIBERMANN R
PATENT ASSIGNEE: MILLENNIUM PHARM INC
PATENT INFO: WO 2002034896 2 May 2002
APPLICATION INFO: WO 2000-US50636 23 Oct 2000
PRIORITY INFO: US 2000-242429 23 Oct 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-479720 [51]

AB DERWENT ABSTRACT:
NOVELTY - Isolated **human myotonic dystrophy** type protein **kinase** polypeptide (PP) (I), designated 13245, comprising a naturally-occurring allelic variant of PP with a fully defined 2053 amino acid sequence (S1) given in the specification encoded by a nucleic acid molecule which hybridizes to a fully defined 6574 or 6159 base pair sequence (S2) given in the specification, is new.

DETAILED DESCRIPTION - Isolated **human myotonic dystrophy** type protein **kinase** polypeptide (PP) (I), designated 13245, comprising a naturally-occurring allelic variant of PP with a fully defined 2053 amino acid sequence (S1) given in the specification encoded by a nucleic acid molecule which hybridizes to a fully defined 6574 or 6159 base pair sequence (S2) given in the specification. In particular (I) comprises:(i) a naturally-occurring allelic variant comprising (S1), PP encoding a nucleic acid molecule which hybridizes to (S2) or its complement under stringent conditions, (ii) a fragment comprising 15 contiguous amino acids of (S1), or (iii) a PP encoded by a nucleic acid which is at least 60% identical to (S2), or its complement. INDEPENDENT CLAIMS are also included for: (1) an isolated nucleic acid molecule (II) encoding (I) or PP comprising S1, comprising a nucleotide sequence at least 60% identical to S2 or a fragment of 300 nucleotides of S2; (2) a host cell (III) containing (II); (3) a non-human mammalian host cell containing (II); (4) an antibody (IV) that selectively binds with (I); (5) producing (I); (6) detecting (M1) the presence of (I) in a sample, by contacting the sample with a compound which selectively binds with (I) and determining whether the compound binds with (I); (7) a kit comprising a compound that selectively binds with (I) or hybridizes with (II); (8) detecting (M2) the presence of (II) in a sample, by contacting the sample with a nucleic acid probe or primer which selectively hybridizes with (II) and determining whether the nucleic acid probe or primer binds with (II); (9) modulating the activity of (I), by contacting (I) or a cell **expressing** (I) with a compound which binds with (I); (10) use of a modulator (V) of the activity of 13245 protein for making a medicament for modulating the ability of a cell to catalyze interconversion of the phosphorylated and de-phosphorylated forms a guanine triphosphate (GTP)ase protein; and (11) making a pharmaceutical composition for modulating e.g. interconversion of the phosphorylated and de-phosphorylated forms of a serine, threonine, or tyrosine residue of a GTPase protein, cell contractility, cell growth, cell conductivity, entry of a cell into the cell cycle, progression of a cell through the cell cycle, mitogenesis, cell metabolism, gene transcription, cytokinesis, cell shape, cell movement, integration of a viral genome into a host cell genome, maintenance of a viral genome within a host cell genome, a cytological change in a virus-infected host cell, virus production in a virus-infected host cell, interaction of a virion with a membrane of a virus-infected host cell, and encapsulation of a virion within a portion of a membrane of a virus-infected host cell, by selecting a test compound useful for modulating phenomenon and combining the test compound with a carrier.

WIDER DISCLOSURE - Disclosed are: (A) vectors containing (II); (B) chimeric or fusion proteins that includes (I) operatively linked to non-13245 polypeptides and its use; (C) screening for compounds that modulate the **expression** of (II); (D) nucleic acid molecule containing a portion of S2 or complement of S2; (E) nucleic acid molecules encoding other 13245 family members having a nucleotide sequence which differ from S2; (F) nucleic acid molecules that is antisense to (II); (G) molecular beacon or detectably labeled oligonucleotide primers and probes; (H) non-human transgenic animals and its use; (I) population of cells from the above animals; (J) analyzing several capture probes or a sample; and (K) making a computer readable record of a sequence of 13245 sequence.

BIOTECHNOLOGY - Preparation: (I) is produced by culturing a mammalian host cell, under conditions in which the nucleic acid molecule is **expressed**. Preferred Polypeptide: (I) further comprises a heterologous amino acid sequence. Preferred Nucleic Acid: (II) further comprises a vector nucleic acid sequence, and a nucleic acid sequence encoding a heterologous PP. Preferred Method: In (M1), the compound that binds with (I) is an antibody. In (M2), the sample comprises mRNA molecules and is contacted with the nucleic acid probe. Preferred Modulator: (V) is an inhibitor of 13245 gene **expression**, preferably an antisense oligonucleotide comprising at least 15 nucleotide residues, which hybridizes under stringent conditions with a transcript (mRNA) of 13245 gene, or with a polynucleotide of S2. (V) does not significantly affect 13245 gene **expression** in the cell. (V) is an agent which inhibits an activity of 69087 protein, preferably an antibody which specifically binds with 69087 protein.

ACTIVITY - Anti-tumor; Virucide; Anti-HIV.

MECHANISM OF ACTION - Gene therapy; Modulator of (I). No supporting data is given.

USE - (I) is useful for identifying a compound which modulates the activity of (I). (I) and (III) are useful for identifying a compound which binds with (I), by determining whether (I) binds with the test compound, by direct detecting of test compound/PP binding, using a competitive binding assay or an assay for 13245-mediated signal transduction. (I) and (III) are useful for assessing whether a test compound is useful for modulating the phenomenon such as cell contractility, cell growth, cell conductivity, and entry of a cell into the cell cycle, by adding the test compound to a first composition comprising (I) or (III), that exhibits 13245 activity, and comparing the activity in the first and second composition that is substantially identical to the first composition except that it does not comprise the test compound, where a difference in the activity indicates that the test compound is useful for modulating the phenomenon. The 13245 activity is GTPase kinase activity, and the composition comprises a cell comprising a nucleic acid encoding the protein, where the nucleic acid is the genome of the cell and comprises the 13245 gene. (I) and (III) are also useful for identifying a compound which is useful for modulating phenomenon (all claimed). 13245 molecules are useful as surrogate markers such as markers of disorders or disease states, as marker for precursors of disease states, as markers for predisposition of disease states, as markers for drug activity, or as markers of pharmacogenomic profile of a subject. 13245 molecules are useful to develop diagnostic and therapeutic agents for prognosticating, diagnosing, preventing, inhibiting, alleviating or curing myotonic dystrophy protein kinase (**MDPK**)-related disorders. (I) is useful to develop diagnostic and therapeutic agents for 13245-mediated or related disorders such as tumorigenesis, tumor growth, tumor metastasis, viral infection of a cell, skeletal muscle disorders (e.g. muscular and myotonic dystrophies), immune disorders and neoplastic disorders. (I) is useful to screen for naturally occurring 13245 substrates, to screen for drugs or compounds which modulate 13245 activity, and to treat disorders characterized by insufficient or excessive production of 13245 protein or production of the protein which have decreased, aberrant or unwanted activity compared to the wild type

protein. Modulator identified by (I) is useful in treating an individual afflicted with disease or disorder characterized by aberrant or unwanted **expression** or activity of 13245 protein or nucleic acid molecule. (II) is useful to **express** a 13245 protein, to detect 13245 mRNA protein in a biological sample, to detect a genetic alteration in a 13245 gene and to modulate 13245 activity. Fragments of (II) are useful in chromosome mapping, tissue typing and aid in forensic identification of a biological sample. (I), (II) and (IV) are useful in screening assays, predictive medicine (diagnostic assays, prognostic assays, monitoring clinical trials and pharmacogenetics) and in treatment methods. (IV) is useful diagnostically to monitor 13245 protein levels in tissues and detect 13245 protein.

ADMINISTRATION - (I) is administered by parenteral (intradermal, subcutaneous, intravenous), oral, transdermal, transmucosal or rectal route or by inhalation at a dose of 0.001-30 mg/kg, preferably 0.1-20 mg/kg and (IV) at a dose of 0.1 mg/kg. Pharmaceutical composition is administered at a dose of 1 mug/kg-500 mg/kg.

EXAMPLE - Identification and characterization of **human myotonic dystrophy** type protein **kinase**, referred as 13245 complementary deoxyribonucleic acid (cDNA) was performed. The human 13245 nucleotide sequence which was 6574 nucleotides in length defined in the specification including non-translated regions, contains a predicted methionine-initiated coding sequence at about nucleotide residues 19-6178 and encoding a 2053 amino acid protein. (148 pages)

L10 ANSWER 7 OF 37 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
DUPLICATE 4
ACCESSION NUMBER: 2003-01696 BIOTECHDS
TITLE: New polypeptide-**human myotonic dystrophy** protein **kinase** 75.90 for treating e.g. myotonic dystrophy, neural disease, tumors, hemopathy, human immunodeficiency virus infection, immunological disease and inflammation; **recombinant** protein production and antagonist use in disease therapy
AUTHOR: MAO Y; XIE Y
PATENT ASSIGNEE: BODE GENE DEV CO LTD SHANGHAI
PATENT INFO: CN 1352281 5 Jun 2002
APPLICATION INFO: CN 2000-127415 10 Nov 2000
PRIORITY INFO: CN 2000-127415 10 Nov 2000; CN 2000-127415 10 Nov 2000
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
OTHER SOURCE: WPI: 2002-628722 [68]
AB DERWENT ABSTRACT:
NOVELTY - The present invention discloses a new kind of polypeptide, **human myotonic dystrophy** protein **kinase** 75.90, polynucleotides encoding the polypeptide and a DNA recombination process to produce the polypeptide. The present invention also discloses applying the polypeptide in treating various diseases, such as myotonic dystrophy, other myodystrophy, neural disease, various tumors, development disturbance, hemopathy, human immunodeficiency virus (HIV) infection, immunological disease and inflammations. The present invention also discloses the antagonist resisting the polypeptide and its treatment effect. The present invention also discloses application of the polynucleotides encoding **human myotonic dystrophy** protein **kinase** 75.90.

L10 ANSWER 8 OF 37 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-18738 BIOTECHDS
TITLE: New polypeptide-**human myotonic dystrophy** protein **kinase** 13.09 for treating e.g. various tumors, inflammation, immunological disease, hemopathy and human immunodeficiency virus infection;

vector-mediated **recombinant** protein gene transfer and **expression** in host cell for use in cancer and HIV virus infection therapy

AUTHOR: MAO Y; XIE Y
PATENT ASSIGNEE: SHANGHAI BIOWINDOW GENE DEV INC
PATENT INFO: CN 1345954 24 Apr 2002
APPLICATION INFO: CN 2000-125356 22 Sep 2000
PRIORITY INFO: CN 2000-125356 22 Sep 2000
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
OTHER SOURCE: WPI: 2002-539353 [58]

AB DERWENT ABSTRACT:
NOVELTY - The present invention discloses a new polypeptide-**human myotonic dystrophy** protein **kinase** 13.09, a polynucleotide encoding the polypeptide and producing the polypeptide by using DNA recombination technology. The invention also discloses curing several diseases, such as myotonic dystrophy, other myodystrophy, nervous disease, various tumors, growth development disturbance disease, inflammation, immunological disease, hemopathy and human immunodeficiency virus (HIV) infection by using the polypeptide. The invention also discloses an antagonist for resisting the polypeptide and its therapeutic action, and application of the polynucleotide encoding the new **human myotonic dystrophy** protein **kinase** 13.09.

L10 ANSWER 9 OF 37 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:625059 BIOSIS
DOCUMENT NUMBER: PREV200200625059
TITLE: Chloride channel mutations in proximal myotonic myopathy: Implications for disease modulating effects.
AUTHOR(S): Ursu, S. F. [Reprint author]; Mao, N. H. [Reprint author]; Lehmann-Horn, F.; Jurkat-Rott, K. [Reprint author]
CORPORATE SOURCE: Applied Physiology, University of Ulm, ULM, Germany
SOURCE: American Journal of Human Genetics, (October, 2002) Vol. 71, No. 4 Supplement, pp. 494. print.
Meeting Info.: 52nd Annual Meeting of the American Society of Human Genetics. Baltimore, MD, USA. October 15-19, 2002. American Society of Human Genetics.
CODEN: AJHGAG. ISSN: 0002-9297.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Dec 2002
Last Updated on STN: 12 Dec 2002

L10 ANSWER 10 OF 37 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
DUPLICATE 5
ACCESSION NUMBER: 2002-00479 BIOTECHDS
TITLE: A novel polypeptide, **human myotonic dystrophy** protein-**kinase**-44 and a polynucleotide sequence encoding the same; plasmid, virus vector-mediated gene transfer and **expression** in host cell, antibody, antisense, DNA probe, DNA primer, DNA microarray, gene chip for HIV virus, cancer etc. gene therapy
AUTHOR: Mao Y; Xie Y
PATENT ASSIGNEE: Shanghai-Biowindow-Gene-Development
LOCATION: Shanghai, People's Republic of China.
PATENT INFO: WO 2001064728 7 Sep 2001
APPLICATION INFO: WO 2001-CN195 26 Feb 2001
PRIORITY INFO: CN 2000-111818 2 Mar 2000
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
OTHER SOURCE: WPI: 2001-550163 [61]

AB An isolated human **recombinant** trophy protein-kinase-44 (I) with a 396 amino acid protein sequence (II) is claimed. Also claimed are: an isolated nucleic acid (1,909 bp DNA sequence) encoding (I); a plasmid or virus vector containing (II); a host cell transformed with the vector; production of (I) by culturing the host cell and recovering (I); an antibody that binds to (I); antagonist and agonist of (I); detection of disease by measuring the **expression** of (I); an antisense of (I); drug screening using (I) for antagonist, agonist, mimics or inhibitors; the use of (I) as DNA primers for amplification reaction and DNA probes as hybridization reaction, or for use in peptide fingerprinting identification, or in producing gene chips or DNA microarrays; and drug compositions containing any of the above. In an example, the **cloning** of (I) was performed by using human fetal RNA and further studied carried out. The above can be used for cancer, hemopathy, HIV virus infection, immunological diseases and various inflammation, myotonic dystrophy, neurogenic disease and developmental disorder diagnosis and gene therapy. (36pp)

L10 ANSWER 11 OF 37 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:482755 BIOSIS
DOCUMENT NUMBER: PREV200100482755
TITLE: Decreased DMPK transcript levels in myotonic dystrophy 1 type IIA muscle fibers.
AUTHOR(S): Eriksson, Maria [Reprint author]; Hedberg, Birgitta; Carey, Nessa; Ansved, Tor
CORPORATE SOURCE: Department of Molecular Medicine and Clinical Neuroscience, Karolinska Institutet, Karolinska Hospital, CMM, Sweden L8: 02; 171 76; Stockholm: maria.eriksson@cmm.ki.se
SOURCE: Biochemical and Biophysical Research Communications, (September 7, 2001) Vol. 286, No. 5, pp. 1177-1182. print. CODEN: BBRCA9. ISSN: 0006-291X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Oct 2001
Last Updated on STN: 23 Feb 2002

AB Myotonic dystrophy 1 is caused by the expansion of a CTG trinucleotide repeat on chromosome 19q13.3. The repeat lies in the 3' untranslated region of the myotonic dystrophy protein kinase gene (DMPK), and it has been hypothesised that the expansion alters the **expression** levels of DMPK and/or its neighbouring genes, DMWD and SIX5. Published data remain controversial, partly due to the mixed cell populations found in most tissues examined. We have microdissected human skeletal muscle biopsies from myotonic dystrophy 1 patients and controls and analysed gene **expression** at this locus for type I and type IIA fibres, using quantitative real-time reverse transcription-polymerase chain reaction. Levels of DMPK **expression** were specifically decreased in the type IIA fibres of myotonic dystrophy patients, below the levels found in controls. This suggests that DMPK **expression** is altered in this disease, suggesting significant pathological consequences.

L10 ANSWER 12 OF 37 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 6
ACCESSION NUMBER: 2001:400475 SCISEARCH
THE GENUINE ARTICLE: 432FK
TITLE: Myotonic dystrophy protein kinase (DMPK) gene **expression** in lymphocytes of patients with myotonic dystrophy
AUTHOR: Depardon F; Cisneros B; Alonso-Vilatela E; Montanez C (Reprint)
CORPORATE SOURCE: Inst Politecn Nacl, CINVESTAV, Dept Genet & Biol Mol, Apdo Postal 14-710, Mexico City 07000, DF, Mexico (Reprint); Inst Politecn Nacl, CINVESTAV, Dept Genet & Biol Mol, Mexico City 07000, DF, Mexico; Inst Nacl Neurol & Neurocirurgia Manuel Velasco S, Dept Neurogenet, Mexico City, DF, Mexico

COUNTRY OF AUTHOR: Mexico
SOURCE: ARCHIVES OF MEDICAL RESEARCH, (MAR-APR 2001) Vol. 32, No. 2, pp. 123-128.
Publisher: ELSEVIER SCIENCE INC, 655 AVENUE OF THE AMERICAS, NEW YORK, NY 10010 USA.
ISSN: 0188-4409.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 28

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background. Myotonic dystrophy (DM) is an autosomal dominant neuromuscular disorder with defects in many tissues, including skeletal muscle myotonia, progressive myopathy, and abnormalities in heart, brain, and endocrine systems. It is associated with a trinucleotide repeat occurring in the 3 ' (UTR) untranslated region of the myotonic dystrophy protein kinase (DMPK) gene, Several studies have been carried out to determine DMPK gene **expression** in muscle and non-muscle tissues.

Methods, DMPK gene **expression** was determined in lymphocytes of adult-onset patients with DM and normal controls. To quantitate total locus **expression** as well as allele-specific mRNA levels, semiquantitative RT-PCR assay was used. Allele-specific **expression** was analyzed using a Bpm1 polymorphism located at exon 10 of the DMPK gene.

Results, In heterozygous patients with DM, we observed a fourfold difference between mRNA levels produced by the Bpm1-undigested allele (187 bp) compared to the Bpm1-digested allele (136 bp). By using (CTG) trinucleotide (with cytosine, thymine, and guanine) expansion polymorphism, it was shown that the down-regulated allele corresponds to the mutant allele. Interestingly, the reduction in the mutant allele-transcript levels is compensated by an increase of the wild-type allele, yielding no significant differences in total locus mRNA amount between patients and normal individuals,

Conclusions. These results suggest that the **expression** of the two alleles at the DMPK locus in lymphocytes is coordinated. The reduction in mutant-allele transcript levels is compensated by an increase in wild-type allele mRNA levels, (C) 2001 IMSS. Published by Elsevier Science Inc.

L10 ANSWER 13 OF 37 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2000391203 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10913253
TITLE: Myotonic dystrophy protein kinase domains mediate localization, oligomerization, novel catalytic activity, and autoinhibition.
AUTHOR: Bush E W; Helmke S M; Birnbaum R A; Perryman M B
CORPORATE SOURCE: Division of Cardiology, Department of Medicine, University of Colorado Health Sciences Center, Denver 80262, USA.
CONTRACT NUMBER: 1RO1HL50715 (NHLBI)
SOURCE: Biochemistry, (2000 Jul 25) 39 (29) 8480-90.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000824
Last Updated on STN: 20020420
Entered Medline: 20000815

AB **Human myotonic dystrophy** protein **kinase** (DMPK) is a member of a novel class of multidomain protein kinases that regulate cell size and shape in a variety of organisms. However, little is currently known about the general properties of DMPK including domain function, substrate specificity, and potential mechanisms of regulation. Two forms of the kinase are **expressed** in muscle,

DMPK-1 and DMPK-2. We demonstrate that the larger DMPK-1 form (the primary translation product) is proteolytically cleaved near the carboxy terminus to generate the smaller DMPK-2 form. We further demonstrate that the coiled-coil domain is required for DMPK oligomerization; coiled-coil mediated oligomerization also correlated with enhanced catalytic activity. DMPK was found to exhibit a novel catalytic activity similar to, but distinct from, related protein kinases such as protein kinase C and A, and the Rho kinases. We observed that **recombinant** DMPK-1 exhibits low activity, whereas the activity of carboxy-terminally truncated DMPK is increased approximately 3-fold. The inhibitory activity of the full-length kinase was mapped to what appears to be a pseudosubstrate autoinhibitory domain at the extreme carboxy terminus of DMPK. To date, endogenous activators of DMPK are unknown; however, we observed that DMPK purified from cells exposed to the G protein activator GTP-gamma-S exhibited an approximately 2-fold increase in activity. These results suggest a general model of DMPK regulation with two main regulatory branches: short-term activation of the kinase in response to G protein second messengers and long-term activation as a result of proteolysis.

L10 ANSWER 14 OF 37 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2001010738 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10970846
TITLE: Cbk1p, a protein similar to the **human myotonic dystrophy kinase**, is essential for normal morphogenesis in Saccharomyces cerevisiae.
AUTHOR: Racki W J; Becam A M; Nasr F; Herbert C J
CORPORATE SOURCE: Centre de Genetique Moleculaire, Laboratoire propre du CNRS, Associe a l'Universite Pierre et Marie Curie, F-91198, Gif-sur-Yvette, France.
SOURCE: EMBO journal, (2000 Sep 1) 19 (17) 4524-32. Journal code: 8208664. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20030308
Entered Medline: 20001024

AB We have studied the CBK1 gene of Saccharomyces cerevisiae, which encodes a conserved protein kinase similar to the **human myotonic dystrophy kinase**. We have shown that the subcellular localization of the protein, Cbk1p, varies in a cell cycle-dependent manner. Three phenotypes are associated with the inactivation of the CBK1 gene: large aggregates of cells, round rather than ellipsoidal cells and a change from a bipolar to a random budding pattern. Two-hybrid and extragenic suppressor studies have linked Cbk1p with the transcription factor Ace2p, which is responsible for the transcription of chitinase. Cbk1p is necessary for the activation of Ace2p and we have shown that the aggregation phenotype is due to a lack of chitinase **expression**. The random budding pattern and the round cell phenotype of the CBK1 deletion strain show that in addition to its role in regulating chitinase **expression** via Ace2p, Cbk1p is essential for a wild-type morphological development of the cell.

L10 ANSWER 15 OF 37 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:430492 BIOSIS
DOCUMENT NUMBER: PREV200000430492
TITLE: Characterization of a monoclonal antibody panel shows that the myotonic dystrophy protein kinase, DMPK, is **expressed** almost exclusively in muscle and heart.
AUTHOR(S): Lam, L. T.; Pham, Y. C. N.; thi Man, Nguyen; Morris, G. E. [Reprint author]

CORPORATE SOURCE: MRIC Biochemistry Group, PP18, North East Wales Institute, Mold Road, Wrexham, LL11 2AW, UK
SOURCE: Human Molecular Genetics, (1 September, 2000) Vol. 9, No. 14, pp. 2167-2173. print.
ISSN: 0964-6906.
DOCUMENT TYPE: Article
LANGUAGE: English
OTHER SOURCE: Genbank-AF250871
ENTRY DATE: Entered STN: 11 Oct 2000
Last Updated on STN: 10 Jan 2002

AB Myotonic dystrophy (DM) is a multisystemic disorder caused by an inherited CTG repeat expansion which affects three genes encoding the DM protein kinase (DMPK), a homeobox protein Six5 and a protein containing WD repeats. Using a panel of 16 monoclonal antibodies against several different DMPK epitopes we detected DMPK, as a single protein of apprx80 kDa, only in skeletal muscle, cardiac muscle and, to a lesser extent, smooth muscle. Many earlier reports of DMPK with different sizes and tissue distributions appear to be due to antibody cross-reactions with more abundant proteins. One such antibody, MANDM1, was used to isolate two related protein kinases, MRCKalpha and beta, from a human brain cDNA library and the shared epitope was located at the catalytic site of DMPK using a phage-displayed random peptide library. The peptide library also identified an epitope shared between DMPK and a 55 kDa muscle-specific protein. The results suggest that effects of the repeat expansion on the DMPK gene may be responsible for muscle and heart features of DM, whereas clinical changes in other tissues may be due to effects on the other two genes.

L10 ANSWER 16 OF 37 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:533022 BIOSIS
DOCUMENT NUMBER: PREV200000533022
TITLE: Myotonic dystrophy and myotonic dystrophy protein kinase.
AUTHOR(S): Ueda, Hideho; Ohno, Shinichi; Kobayashi, Takayoshi [Reprint author]
CORPORATE SOURCE: Department of Neurology, Nakano General Hospital, 4-59-16 Chuo, Nakano-ku, Tokyo, 164-8607, Japan
SOURCE: Progress in Histochemistry and Cytochemistry, (2000) Vol. 35, No. 3, pp. 187-251. print.
CODEN: PHCCAS. ISSN: 0079-6336.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 2000
Last Updated on STN: 11 Jan 2002

L10 ANSWER 17 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:318246 HCAPLUS
DOCUMENT NUMBER: 135:302237
TITLE: Skeletal myopathy in mice over-**expressing** the **human myotonic** **dystrophy** protein **kinase** (DMPK) gene
AUTHOR(S): Narang, Monica A.; Waring, James D.; Sabourin, Luc A.; Rajcan-Separovic, Evica; Parry, David; Jirik, Frank; Korneluk, Robert G.
CORPORATE SOURCE: Soulange Gauthier Karsh Molecular Genetics Laboratory, Children's Hospital of Eastern, Ottawa, ON, K1H 8L1, Can.
SOURCE: Gene Function & Disease (2000), 1(3-4), 134-144
CODEN: GFDEAS; ISSN: 1438-7506
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Myotonic dystrophy (DM) is caused by the expansion of a trinucleotide repeat located in the 3'-untranslated region of a Ser-Thr kinase (DMPK),

such that repeat size corresponds with severity of disease and age of onset. The mechanism by which this mutation causes DM remains unclear. Recent reports indicate that over-**expression** of DMPK in murine C2C12 myoblasts inhibits myogenesis, reminiscent of the marked immaturity observed in DM patient muscle. Accordingly, the authors generated transgenic mice over-**expressing** the human DMPK gene with **expression** enhancing matrix attachment region (MAR) sequences. These mice show substantial over-**expression** of human DMPK transcript and protein in brain, skeletal muscle, tongue, and eye - tissues typically affected in DM. Cryostat sections of skeletal muscle from these transgenic animals revealed diagnostic hallmarks of DM including increased centronucleation, type 1 fiber atrophy and ringed fibers. Addnl., primary myoblasts established from these mice showed reduced fusion potential indicating a delay or defect in myoblast differentiation. These results suggest that over-**expression** of the human DMPK gene in these mice confers a skeletal muscle pathol. similar to that seen in DM patients.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 18 OF 37 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1999:461690 BIOSIS
DOCUMENT NUMBER: PREV199900461690
TITLE: Visualization of double-stranded RNAs from the myotonic dystrophy protein kinase gene and interactions with CUG-binding protein.
AUTHOR(S): Michalowski, Susan; Miller, Jill W.; Urbinati, Carl R.; Paliouras, Miltiadis; Swanson, Maurice S.; Griffith, Jack [Reprint author]
CORPORATE SOURCE: Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599, USA
SOURCE: Nucleic Acids Research, (Sept. 1, 1999) Vol. 27, No. 17, pp. 3534-3542. print.
CODEN: NARHAD. ISSN: 0305-1048.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Nov 1999
Last Updated on STN: 1 Nov 1999

AB Myotonic dystrophy (DM) is associated with a (CTG)n triplet repeat expansion in the 3'-untranslated region of the myotonic dystrophy protein kinase (DMPK) gene. Using electron microscopy, we visualized large RNAs containing up to 130 CUG repeats and studied the binding of purified CUG-binding protein (CUG-BP) to these RNAs. Electron microscopic examination revealed perfect double-stranded (ds)RNA segments whose lengths were that expected for duplex RNA. The RNA dominant mutation model for DM pathogenesis predicts that the expansion mutation acts at the RNA level by forming long dsRNAs that sequester certain RNA-binding proteins. To test this model, we examined the subcellular distribution and RNA-binding properties of CUG-BP. While previous studies have demonstrated that mutant DMPK transcripts accumulate in nuclear foci, the localization pattern of CUG-BP in both normal and DM cells was similar. Although CUG-BP in nuclear extracts preferentially photo-crosslinked to DMPK transcripts,this binding was not proportional to (CUG)n repeat size. Moreover, CUG-BP localized to the base of the RNA hairpin and not along the stem, as visualized by electron microscopy. These results provide the first visual evidence that the DM expansion forms an RNA hairpin structure and suggest that CUG-BP is unlikely to be a sequestered factor.

L10 ANSWER 19 OF 37 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 9

ACCESSION NUMBER: 2000031276 EMBASE
TITLE: [Autosomal dominant myotonic dystrophies]. AUTOSOMAL DOMINANTE MYOTONE DYSTROPHIEN.
AUTHOR: Finsterer J.
CORPORATE SOURCE: Dr. J. Finsterer, Postfach 348, A-1180 Vienna, Austria.

fij@2nr.nkr.magwien.gv.at
SOURCE: Nervenheilkunde, (1999) 18/10 (542-546).
Refs: 26
ISSN: 0722-1541 CODEN: NERVDI
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
022 Human Genetics
LANGUAGE: German
SUMMARY LANGUAGE: English; German
AB Myotonic dystrophy is clinically and genetically heterogenous and comprises classical myotonic dystrophy (MD), type 2 myotonic dystrophy (MD2) and proximal myotonic myopathy (PROMM). MD is caused by an unstable CTG- repeat in an untranslated region of the myotonic dystrophy phospho-kinase (**MDPK**) gene on chromosome 19q13.3. Both, MD2 and PROMM derive from mutations in a yet unidentified gene, mapped to chromosome 3q21. It is assumed that the CTG-expansion affects not only the **expression** of the **MDPK** and neighbouring genes but, according to the RNA metabolism defect hypothesis, also the processing and translation of the **MDPK** and other mRNAs. These mechanisms may explain the severe and pleomorphic phenotype of MD.

L10 ANSWER 20 OF 37 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:174817 BIOSIS
DOCUMENT NUMBER: PREV199900174817
TITLE: Characterization of the **expression** of DMPK and SIX5 in the human eye and implications for pathogenesis in myotonic dystrophy.
AUTHOR(S): Winchester, Catherine L.; Ferrier, Rod K.; Sermoni, Adriana; Clark, Brian J.; Johnson, Keith J. [Reprint author]
CORPORATE SOURCE: Division of Molecular Genetics, Institute of Biomedical and Life Sciences, University of Glasgow, Anderson College, 56 Dumbarton Road, Glasgow, G11 6NU, UK
SOURCE: Human Molecular Genetics, (March, 1999) Vol. 8, No. 3, pp. 481-492. print.
ISSN: 0964-6906.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 May 1999
Last Updated on STN: 5 May 1999
AB The pathogenic mechanisms underlying myotonic dystrophy (DM), which results from a (CTG)n repeat expansion mutation in the 3'-untranslated region (3'-UTR) of the myotonic dystrophy protein kinase gene (DMPK), remain obscure. The multisystemic nature and variable **expressivity** of the symptoms are unlikely to be explained by a defect in this gene alone. However, the location of the DM-associated (CTG)n repeat in the promoter region of SIX5, immediately downstream of DMPK, implicates it as a second candidate with a pathological role in DM. We hypothesize that dysfunction of SIX5, which is homologous to the Drosophila eye development gene sine oculis (so), is primarily responsible for the ophthalmic features of DM. We report an **expression** pattern for SIX5 in the normal adult eye that matches the sites of the ocular pathology in DM. SIX5 transcripts were detected in the adult corneal epithelium and endothelium, lens epithelium, ciliary body epithelia, cellular layers of the retina and the sclera. SIX5 **expression** was not detected in fetal eyes. We also report a restricted but partially overlapping **expression** pattern for DMPK transcripts and DMPK protein in normal fetal and adult eyes. DMPK transcripts were detected in fetal eyes and in adult conjunctival and corneal epithelia, uvea, cellular layers of the retina, optic nerve and in the sclera. DMPK protein was detected in the adult retina, conjunctival and ciliary body epithelia and in the smooth muscle of the ciliary body, pupillary sphincter and uveal blood vessels. We propose that the

expression patterns of these two genes indicate their relative contribution to the ophthalmological dysfunction seen in DM. Furthermore, the **expression** of SIX5 and not DMPK in the adult lens implicates a role for SIX5 dysfunction in the development of adult onset cataracts, the most frequently occurring eye phenotype in DM.

L10 ANSWER 21 OF 37 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:222195 BIOSIS
DOCUMENT NUMBER: PREV199900222195
TITLE: Lens epithelial changes and mutated gene **expression** in patients with myotonic dystrophy.
AUTHOR(S): Abe, Toshiaki [Reprint author]; Sato, Masami; Kuboki, Junko; Kano, Tetsuya; Tamai, Makoto
CORPORATE SOURCE: Department of Ophthalmology, Tohoku University School of Medicine, 1-1 Seiryoumachi Aobaku Sendai, Miyagi, 980-8594, Japan
SOURCE: British Journal of Ophthalmology, (April, 1999) Vol. 83, No. 4, pp. 452-457. print.
CODEN: BJOPAL. ISSN: 0007-1161.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jun 1999
Last Updated on STN: 7 Jun 1999

AB Aims-Examination of the **expression** of the mutated allele of myotonic dystrophy protein kinase gene and lens epithelial cell changes in patients with myotonic dystrophy. Methods-Six eyes from three patients with myotonic dystrophy underwent cataract surgery. The lens epithelium was photographed to examine the morphological changes. mRNAs were extracted to determine myotonic dystrophy protein kinase gene **expression** in the lens epithelium and peripheral blood. Age matched lens epithelial cells from senile cataracts were used as controls. Results-All eyes showed iridescent or posterior subcapsular lens opacity. The **expression** of the myotonic dystrophy protein kinase gene with trinucleotide repeat expansion was evaluated by reverse transcriptase polymerase chain reaction, Southern blotting, and sequence analysis. Lens epithelial cell densities were extremely reduced in the patients compared with the control group. Conclusion-To the authors' knowledge, this is the first report to describe the relation between lens epithelial cell changes and mutated gene **expression** in patients with myotonic dystrophy. The gene may be mitotically unstable in the lens epithelial cells; it may influence cell density and lens epithelial function, and it may lead to the development of typical subcapsular lens opacity.

L10 ANSWER 22 OF 37 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 1999133868 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9950369
TITLE: Unstable expansion of the CAG trinucleotide repeat in MAB21L1: report of a second pedigree and effect on protein **expression**.
AUTHOR: Margolis R L; Stine O C; Ward C M; Franz M L; Rosenblatt A; Callahan C; Sherr M; Ross C A; Potter N T
CORPORATE SOURCE: Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, USA.
CONTRACT NUMBER: MH02175 (NIMH)
MH50763 (NIMH)
NS34172 (NINDS)
SOURCE: Journal of medical genetics, (1999 Jan) 36 (1) 62-4.
Journal code: 2985087R. ISSN: 0022-2593.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990504

Last Updated on STN: 19990504
Entered Medline: 19990421

AB MAB21L1, originally termed CAGR1, is the human homologue of the C. elegans cell fate determining gene mab21. MAB21L1, mapped to 13q13, contains a highly polymorphic 5' untranslated CAG repeat that normally ranges from six to 31 triplets in length. A pedigree has been previously reported in which the repeat length is expanded to 45-50 triplets and is transmitted unstably between generations; the expansion did not correlate to a clinical phenotype but did exhibit somatic mosaicism. We now report a second pedigree with an expanded and unstably transmitted MAB21L1 CAG repeat of similar length. The expansion is not clearly associated with a clinical phenotype, though the complexity of the pedigree renders any conclusion concerning phenotype-genotype relationships speculative. The expansion did not result in decreased **expression** of MAB21L1 protein. The length, C-G rich composition, somatic mosaicism, and unstable transmission of the expanded CAG repeat in MAB21L1 resemble the premutations observed in other genes, such as FMR1 and **MDPK**, in which longer expanded repeats are associated with a clinical phenotype. This raises the possibility that longer expansions in the MAB21L1 repeat may also be associated with a clinical phenotype.

L10 ANSWER 23 OF 37 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:509178 BIOSIS
DOCUMENT NUMBER: PREV199900509178
TITLE: Transgenic mice carrying the human DM region: A model for CTG repeat intergenerational and somatic instability analysis of the CTG repeat amplification influence in transgenic mice.
AUTHOR(S): Junien, C. [Reprint author]; Seznec, H. [Reprint author]; Lia, A.-S. [Reprint author]; Agbulut, O.; Duros, C. [Reprint author]; Fouquet, C. [Reprint author]; Radvany, H.; Gourdon, G. [Reprint author]
CORPORATE SOURCE: Inserm UR383, Hopital Necker Enfants Malades, Paris Cedex, 15, France
SOURCE: American Journal of Human Genetics, (Oct., 1999) Vol. 65, No. 4, pp. A29. print.
Meeting Info.: 49th Annual Meeting of the American Society of Human Genetics. San Francisco, California, USA. October 19-23, 1999. The American Society of Human Genetics.
CODEN: AJHGAG. ISSN: 0002-9297.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Slide)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Dec 1999
Last Updated on STN: 3 Dec 1999

L10 ANSWER 24 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:759807 HCAPLUS
DOCUMENT NUMBER: 130:121219
TITLE: Localization of myotonic dystrophy protein kinase in human and rabbit tissues using a new panel of monoclonal antibodies
AUTHOR(S): Pham, Y. C. N.; Nguyen thi Man; Lam, Le Thanh; Morris, G. E.
CORPORATE SOURCE: MRIC Biochemistry Group, NE Wales Institute, Wrexham, LL11 2AW, UK
SOURCE: Human Molecular Genetics (1998), 7(12), 1957-1965
CODEN: HMGEE5; ISSN: 0964-6906
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB There is considerable confusion in the literature about the size of the myotonic dystrophy protein kinase (DMPK) and its localization within

tissues. We have used a new panel of monoclonal antibodies (mAbs) to begin to resolve these issues, which are important for understanding the possible role of DMPK in myotonic dystrophy. Antisera raised against the catalytic and coil domains of DMPK recognized a major 55 kDa protein and a minor 72-80 kDa doublet on western blots of human skeletal muscle. Ten mAbs, five against the catalytic domain and five against the coil region, recognized only the 72-80 kDa doublet. The 72 kDa protein was present in all tissues tested, whereas the 80 kDa component was variably **expressed**, mainly in skeletal and cardiac muscles. The 72 kDa protein was absent in a DMPK knockout mouse and was greatly increased in a transgenic mouse overexpressing human DMPK, confirming its identity as authentic DMPK. Two mAbs against the catalytic domain recognized only the more abundant 55 kDa protein, which was found only in skeletal muscle. Nine out of 10 mAbs located DMPK to intercalated disks in human heart, an affected tissue in myotonic dystrophy. However, co-localization of DMPK with acetylcholine receptors at neuromuscular junctions was not observed with any of the mAbs. Subcellular fractionation and sedimentation anal. suggest that a major proportion of the DMPK in skeletal muscle and brain is cytosolic.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 25 OF 37 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 1998:261241 SCISEARCH
THE GENUINE ARTICLE: ZE078
TITLE: Ribozyme-mediated trans-splicing of a trinucleotide repeat
AUTHOR: Phylactou L A (Reprint); Darrah C; Wood M J A
CORPORATE SOURCE: UNIV OXFORD, DEPT HUMAN ANAT, S PARKS RD, OXFORD OX1 3QX, ENGLAND (Reprint)
COUNTRY OF AUTHOR: ENGLAND
SOURCE: NATURE GENETICS, (APR 1998) Vol. 18, No. 4, pp. 378-381. Publisher: NATURE PUBLISHING CO, 345 PARK AVE SOUTH, NEW YORK, NY 10010-1707. ISSN: 1061-4036.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 30

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Trinucleotide repeat expansions (TREs) are a recently described class of mutations characterized by a change in the size of the genomic fragment due to amplification of the repeated unit. A number of diseases have been attributed to TRE, including Huntington disease and myotonic dystrophy (DM; refs 1-3), but attempts at genetic therapy have yet to prove successful. A potential therapeutic approach would be to repair the expanded repeat using the trans-splicing ability of group I intron ribozymes(4). We have used DM as a model to test this hypothesis. A group I intron ribozyme (DMPK-RZ1) was designed to modify the TRE at the 3' end of the **human myotonic dystrophy** protein **kinase** (DMPK) transcript(5-8). DMPK-RZ1 was shown to ligate a small DMPK mRNA fragment, contained within the ribozyme, to a simple DMPK-target RNA in vitro. It also modified a larger target transcript, leading to replacement of twelve repeats with five repeats, both in vitro and in mammalian cells. Finally, this ribozyme successfully replaced the 3' end of endogenous DMPK mRNA in fibroblasts with a different 3' region. Ribozyme-mediated RNA repair may thus form a novel therapeutic strategy for diseases associated with repeat expansions.

L10 ANSWER 26 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:514386 HCAPLUS
DOCUMENT NUMBER: 129:311386
TITLE: **Expression** of the **human myotonic dystrophy kinase** (dmk) gene in transgenic mice

AUTHOR(S): Narang, Monica Ajoo
CORPORATE SOURCE: Univ. of Ottawa, Ottawa, ON, Can.
SOURCE: (1997) 151 pp. Avail.: UMI, Order No. DANQ26136
From: Diss. Abstr. Int., B 1998, 59(3), 986
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L10 ANSWER 27 OF 37 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 97376687 EMBASE
DOCUMENT NUMBER: 1997376687
TITLE: Genghis Khan (Gek) as a putative effector for Drosophila Cdc42 and regulator of actin polymerization.
AUTHOR: Luo L.; Lef T.; Tsai L.; Tang G.; Jan L.Y.; Yuh Nung Jan
CORPORATE SOURCE: L. Luo, Department of Biological Sciences, Stanford University, Stanford, CA 94305, United States. Huo@stanford.edu
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1997) 94/24 (12963-12968). Refs: 41
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The small GTPases Cdc42 and Rac regulate a variety of biological processes, including actin polymerization, cell proliferation, and JNK/mitogen-activated protein kinase activation, conceivably via distinct effectors. Whereas the effector for mitogen-activated protein kinase activation appears to be p65(PAK), the identity of effector(s) for actin polymerization remains unclear. We have found n putative effector for Drosophila Cdc42, Genghis Khan (Gek), which binds to Dcdc42 in a GTP-dependent and effector domain-dependent manner. Gek contains a predicted serine/threonine kinase catalytic domain that is 63% identical to **human myotonic dystrophy** protein **kinase** and has protein kinase activities. It also possesses n large coiled-coil domain, a putative phorbol ester binding domain, a pleckstrin homology domain, and a Cdc42 binding consensus sequence that is required for its binding to Dedc42. To study the in vivo function of gek, we generated mutations in the Drosophila gek locus. Egg chambers homozygous for gek mutations exhibit abnormal accumulation of F-actin and are defective in producing fertilized eggs. These phenotypes can be rescued by a wild-type grk transgene. Our results suggest that this multidomain protein kinase is an effector for the regulation of actin polymerization by Cdc42.

L10 ANSWER 28 OF 37 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 97:240814 SCISEARCH
THE GENUINE ARTICLE: WN186
TITLE: Demonstration of a retinitis pigmentosa (RP) phenotype in adult transgenic mice over-**expressing** the **human myotonic dystrophy** protein **kinase** (DMK)
AUTHOR: Daneshvar H (Reprint); Damji K F; Narang M; Hill V; Waring J; Brownstein S; Korneluk R
CORPORATE SOURCE: UNIV OTTAWA, INST EYE, OTTAWA, ON, CANADA; GENET MOL LAB, OTTAWA, ON, CANADA; CHILDRENS HOSP EASTERN ONTARIO, OTTAWA, ON K1H 8L1, CANADA
COUNTRY OF AUTHOR: CANADA
SOURCE: INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE, (15 MAR 1997) Vol. 38, No. 4, Part 1, pp. 1457-1457.
Publisher: LIPPINCOTT-RAVEN PUBL, 227 EAST WASHINGTON SQ,

PHILADELPHIA, PA 19106.
ISSN: 0146-0404.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 0

L10 ANSWER 29 OF 37 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 97195483 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9042856
TITLE: Caenorhabditis elegans LET-502 is related to Rho-binding kinases and **human myotonic dystrophy kinase** and interacts genetically with a homolog of the regulatory subunit of smooth muscle myosin phosphatase to affect cell shape.
AUTHOR: Wissmann A; Ingles J; McGhee J D; Mains P E
CORPORATE SOURCE: University of Calgary, Department of Medical Biochemistry, Alberta, Canada.. wissmann@acs.ucalgary.ca
SOURCE: Genes & development, (1997 Feb 15) 11 (4) 409-22.
Journal code: 8711660. ISSN: 0890-9369.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U14989; GENBANK-U85515; GENBANK-U86640; GENBANK-X71057; GENBANK-Z30329; GENBANK-Z30330
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970407
Last Updated on STN: 20020420
Entered Medline: 19970324

AB We have identified two genes associated with the hypodermal cell shape changes that occur during elongation of the Caenorhabditis elegans embryo. The first gene, called let-502, encodes a protein with high similarity to Rho-binding Ser/Thr kinases and to **human myotonic dystrophy kinase** (DM-**kinase**). Strong mutations in let-502 block embryonic elongation, and let-502 reporter constructs are **expressed** in hypodermal cells at the elongation stage of development. The second gene, mel-11, was identified by mutations that act as extragenic suppressors of let-502. mel-11 encodes a protein similar to the 110- to 133-kD regulatory subunits of vertebrate smooth muscle myosin-associated phosphatase (PP-1M). We suggest that the LET-502 kinase and the MEL-11 phosphatase subunit act in a pathway linking a signal generated by the small GTP-binding protein Rho to a myosin-based hypodermal contractile system that drives embryonic elongation. LET-502 may directly regulate the activity of the MEL-11 containing phosphatase complex and the similarity between LET-502 and DM-kinase suggests a similar function for DM-kinase.

L10 ANSWER 30 OF 37 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1997:286469 BIOSIS
DOCUMENT NUMBER: PREV199799585672
TITLE: Demonstration of a retinitis pigmentosa (RP) phenotype in adult transgenic mice over-**expressing** the **human myotonic dystrophy** protein **kinase** (DMK).
AUTHOR(S): Danesvar, H. [Reprint author]; Damji, K. F. [Reprint author]; Narang, M.; Hill, V. [Reprint author]; Waring, J.; Brownstein, S. [Reprint author]; Korneluk, R.
CORPORATE SOURCE: Univ. Ottawa Eye Inst., Mol. Genet. Lab., Ottawa, Canada
SOURCE: Investigative Ophthalmology and Visual Science, (1997) Vol. 38, No. 4 PART 1-2, pp. S312.
Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology, Parts 1-2. Fort Lauderdale, Florida, USA. May 11-16, 1997.

CODEN: IOVSDA. ISSN: 0146-0404.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Jul 1997
Last Updated on STN: 3 Jul 1997

L10 ANSWER 31 OF 37 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 96132955 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8550617
TITLE: Overexpression of myotonic dystrophy kinase in BC3H1 cells induces the skeletal muscle phenotype.
AUTHOR: Bush E W; Taft C S; Meixell G E; Perryman M B
CORPORATE SOURCE: Department of Medicine, University of Colorado Health Sciences Center, Denver 80262, USA.
CONTRACT NUMBER: 1RO1HL50715 (NHLBI)
SOURCE: Journal of biological chemistry, (1996 Jan 5) 271 (1) 548-52.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-Z28822; GENBANK-Z33441
ENTRY MONTH: 199602
ENTRY DATE: Entered STN: 19960306
Last Updated on STN: 20000303
Entered Medline: 19960220

AB Myotonic muscular dystrophy is an autosomal dominant defect that produces muscle wasting, myotonia, and cardiac conduction abnormalities. The myotonic dystrophy locus codes for a putative serine-threonine protein kinase of unknown function. We report that overexpression of **human myotonic dystrophy** protein **kinase** induces the **expression** of skeletal muscle-specific genes in undifferentiated BC3H1 muscle cells. BC3H1 **clones expressing** myotonic dystrophy kinase appear equivalent to differentiated cells with respect to **expression** of myogenin, retinoblastoma tumor supressor gene, M creatine kinase, beta-tropomyosin, and vimentin. In addition, differential display analysis demonstrates that the pattern of gene **expression** exhibited by myotonic dystrophy kinase-**expressing** cells is essentially identical to that of differentiated BC3H1 muscle cells. These observations suggest that myotonic dystrophy kinase may function in the myogenic pathway.

L10 ANSWER 32 OF 37 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 96:126812 SCISEARCH
THE GENUINE ARTICLE: TT848
TITLE: THE SEQUENCE OF 36.8 KB FROM THE LEFT ARM OF CHROMOSOME-XIV REVEALS 24 COMPLETE OPEN READING FRAMES - 18 CORRESPOND TO NEW GENES, ONE OF WHICH ENCODES A PROTEIN SIMILAR TO THE **HUMAN MYOTONIC-DYSTROPHY KINASE**
AUTHOR: NASR F; BECAM A M; HERBERT C J (Reprint)
CORPORATE SOURCE: UNIV PARIS 06, CTR GENET MOLEC, CNRS, LAB PROPRE, F-91198 GIF SUR YVETTE, FRANCE (Reprint); UNIV PARIS 06, CTR GENET MOLEC, CNRS, LAB PROPRE, F-91198 GIF SUR YVETTE, FRANCE
COUNTRY OF AUTHOR: FRANCE
SOURCE: YEAST, (FEB 1996) Vol. 12, No. 2, pp. 169-175.
ISSN: 0749-503X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; AGRI
LANGUAGE: ENGLISH

REFERENCE COUNT: 28

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We have determined the complete nucleotide sequence of a 36.8 kb segment from the left arm of chromosome XIV carried by the cosmid 14-11. The sequence encodes the 5' coding region of the PSD1 gene, the 3' coding region of an unknown gene and 24 complete open reading frames, of which 18 correspond to new genes and six (SKO1, SCL41A, YGP1, YCK2, RPC31 and MFA2) have been sequenced previously. Of the 24 new genes, five show significant similarities to sequences present in the databanks. These include elongation factors 2 and the **human myotonic dystrophy kinase**. The sequence has been deposited in the EMBL databank under the Accession Number X92517.

L10 ANSWER 33 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:118617 HCAPLUS
DOCUMENT NUMBER: 124:199623
TITLE: Localization of myotonic dystrophy protein kinase in skeletal muscle and its alteration with disease
AUTHOR(S): Dunne, Patrick W.; Ma, Lei; Casey, Douglas L.; Harati, Yadollah; Epstein, Henry F.
CORPORATE SOURCE: Department of Neurology, Baylor College of Medicine, Houston, TX, 77030, USA
SOURCE: Cell Motility and the Cytoskeleton (1996), 33(1), 52-63
CODEN: CMCYEO; ISSN: 0886-1544
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Myotonic dystrophy (DM) is an autosomal dominant disorder which affects skeletal muscle, heart, eye lens, brain, and endocrine functions. The disease-causing mutations are expansions of the triplet repeat CTG in the 3' untranslated region of a locus which encodes a serine/threonine protein kinase that represents a new family of protein kinases. A monoclonal antibody to a **recombinant** DM protein kinase (mAb DM-1) reacts specifically with the 64 kDa isoform of DM protein kinase in type I fibers in skeletal muscle, the fiber type which characteristically atrophies in the disease. Within type I fibers of normal muscle the isoform may be localized with mAb DM-1 to the triad region. In the DM disease state, the enzyme is redistributed to the pathol. characteristic peripheral sarcoplasmic masses. In markedly affected human distal myotonic muscle, the levels of the 64 kDa DM kinase isoform are elevated relative to slow skeletal myosin heavy chain. These results suggest that, consistent with the dominant clin. phenotype, the localization and accumulation of the 64 kDa isoform are altered in the heterozygous disease state.

L10 ANSWER 34 OF 37 MEDLINE on STN DUPLICATE 13

ACCESSION NUMBER: 96094284 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7493923
TITLE: A novel serine/threonine kinase binding the Ras-related RhoA GTPase which translocates the kinase to peripheral membranes.
AUTHOR: Leung T; Manser E; Tan L; Lim L
CORPORATE SOURCE: Glaxo-IMCB Group, Institute of Molecular and Cell Biology, National University of Singapore, Kent Ridge, Singapore.
SOURCE: Journal of biological chemistry, (1995 Dec 8) 270 (49) 29051-4.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-L08835; GENBANK-L39837; GENBANK-P28867; GENBANK-P38679; GENBANK-U38481
ENTRY MONTH: 199601

ENTRY DATE: Entered STN: 19960217
Last Updated on STN: 20020420
Entered Medline: 19960111

AB We previously reported the **cloning** of a serine/threonine kinase, PAK (for p21 (Cdc42/Rac)-activated kinase), which binds to the Ras-related GTPases Cdc42Hs and Rac1 (Manser, E., Leung, T., Salihuddin, H., Zhao, Z-s., and Lim, L. (1994) Nature 367, 40-46). These p21 proteins together with RhoA comprise the Rho subfamily of proteins that are involved in morphological events. We now report the isolation of a rat cDNA encoding a 150-kDa protein, which specifically binds RhoA in its GTP form and contains an N-terminal serine/threonine kinase domain highly related to the **human myotonic dystrophy kinase** and a cysteine-rich domain toward the C terminus. The RhoA binding domain is unrelated to other p21 binding domains. Antibody raised against the kinase domain of the predicted protein, termed ROK alpha (for ROK alpha, RhoA-binding kinase), recognized a ubiquitous 150-kDa protein. The brain p150 purified by affinity chromatography with RhoA exhibited serine/threonine kinase activity. In cultured cells, immunoreactive p150 was recruited to membranes upon transfection with dominant positive RhoAV14 mutant and was localized with actin microfilaments at the cell periphery. These results are consistent with a role for the kinase ROK alpha as an effector for RhoA.

L10 ANSWER 35 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:613945 HCAPLUS
DOCUMENT NUMBER: 123:50541
TITLE: Characterization of myotonic dystrophy kinase (DMK) protein in human and rodent muscle and central nervous tissue
AUTHOR(S): Whiting, Elisabeth J.; Waring, James D.; Tamai, Katsuyuki; Somerville, Martin J.; Hincke, Maxwell; Staines, William A.; Ikeda, Joh-E.; Korneluk, Robert G.
CORPORATE SOURCE: Dep. Microbiol. Immunol., Univ. Ottawa, Ottawa, ON, Can.
SOURCE: Human Molecular Genetics (1995), 4(6), 1063-72
CODEN: HMGEE5; ISSN: 0964-6906
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Myotonic dystrophy (DM) is the most common form of inherited neuromuscular disease in adults and is characterized by progressive muscle wasting and myotonia. The mutation responsible for DM has been identified as the amplification of a polymorphic (CTG)n repeat in the 3' untranslated region of a gene encoding a serine/threonine kinase (DMK). We have produced a polyclonal rabbit antibody preparation against a fusion protein encoding the C-terminal amino acids 471-629 of the human DMK gene. This antibody specifically detects products of both full length and truncated human DMK genes **expressed** in bacteria and in insect cells. On immunoblots, we observed protein species of .apprx.74 and 82 kDa in cardiac muscle, skeletal muscle, ependyma and choroid plexus. By immunofluorescence, DMK was found to localize post-synaptically at the neuromuscular junction of skeletal muscle, at intercalated disks of cardiac tissue and at the apical membrane of the ependyma and choroid plexus. We have also detected two to three species (.apprx.45-50 kDa) in other regions of the brain. Synaptic localization of DMK in the cerebellum, hippocampus, midbrain and medulla was noted. These results suggest that DMK plays a specialized role in intercellular communication.

L10 ANSWER 36 OF 37 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 95212904 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7698644
TITLE: The Drosophila tumor suppressor gene warts encodes a homolog of **human myotonic**

dystrophy kinase and is required for the control of cell shape and proliferation.

AUTHOR: Justice R W; Zilian O; Woods D F; Noll M; Bryant P J

CORPORATE SOURCE: Developmental Biology Center, University of California, Irvine 92717.

CONTRACT NUMBER: CA-09338 (NCI)

SOURCE: Genes & development, (1995 Mar 1) 9 (5) 534-46.
Journal code: 8711660. ISSN: 0890-9369.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-L39837

ENTRY MONTH: 199505

ENTRY DATE: Entered STN: 19950510
Last Updated on STN: 20020420
Entered Medline: 19950502

AB Homozygous loss of the warts (wts) gene of Drosophila, caused by mitotic recombination in somatic cells, leads to the formation of cell **clones** that are fragmented, rounded, and greatly overgrown compared with normal controls. Therefore, the gene is required for the control of the amount and direction of cell proliferation as well as for normal morphogenesis. The absence of wts function also results in apical hypertrophy of imaginal disc epithelial cells. Secretion of cuticle over and between the domed apical surfaces of these cells leads to a honeycomb-like structure and gives the superficial wart-like phenotype of mitotic **clones** on the adult. One wts allele allows survival of homozygotes to the late larval stage, and these larvae show extensive imaginal disc overgrowth. Because of the excess growth and abnormalities of differentiation that follow homozygous loss, we consider wts to be a tumor suppressor gene. The wts gene is defined by the breakpoints of overlapping deficiencies in the right telomeric region of chromosome 3, region 100A, and by lethal P-element insertions and excisions. It encodes a protein kinase that is most similar to **human myotonic dystrophy kinase**, the Neurospora cot-1 protein kinase, two cell-cycle regulated kinases of yeast, and several putative kinases from plants. These proteins define a new subfamily of protein kinases that are closely related to but distinct from the cyclic AMP-dependent kinases. Although myotonic dystrophy is defined by a neuromuscular disorder, it is sometimes associated with multiple pilomatrixomas, which are otherwise rare epithelial tumors, and with other tumors including neurofibromas and parathyroid adenomas. Our results raise the possibility that homozygous loss of the myotonic dystrophy kinase may contribute to the development of these tumors.

L10 ANSWER 37 OF 37 MEDLINE on STN DUPLICATE 15

ACCESSION NUMBER: 94355306 MEDLINE

DOCUMENT NUMBER: PubMed ID: 8075083

TITLE: Phosphorylation reactions of **recombinant human myotonic dystrophy** protein **kinase** and their inhibition.

AUTHOR: Dunne P W; Walch E T; Epstein H F

CORPORATE SOURCE: Department of Neurology, Baylor College of Medicine, Houston, Texas 77030.

CONTRACT NUMBER: 1R01 EY09708-01 (NEI)

SOURCE: Biochemistry, (1994 Sep 6) 33 (35) 10809-14.
Journal code: 0370623. ISSN: 0006-2960.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199410

ENTRY DATE: Entered STN: 19941013
Last Updated on STN: 20020420

Entered Medline: 19941004

AB The predicted protein kinase activity of the **cloned** gene product of the human myotonic dystrophy locus has been experimentally verified. Affinity-purified **recombinant** DM protein kinase became phosphorylated itself and transphosphorylated histone H1. These activities were not present in the bacterial host cells and were exhibited by DMPK and DMPKH, **recombinant** proteins which contain the protein kinase domain but exhibit distinct sizes, 43 and 66 kDa, respectively. DMPKH was further purified by velocity sedimentation on sucrose gradients; both activities migrated with the **recombinant** protein at 41 S, consistent with discrete multimeric particles. Phosphoamino acid analysis showed that threonine (predominantly) and serine were phosphorylated in both DMPKH and histone H1. Although PKA and PKC are the known types of protein kinase with closest sequence homology to the DM protein kinase domain, purified DMPKH was inhibited by 4 mM but not 0.04-0.4 mM H7 and H8, which inhibit PKA and PKC with Ki's of 0.4-15 microM. Specific inhibitors of other classes of multifunctional serine/threonine protein kinases such as casein kinases I (CKI-7) and II (heparin) and calcium/calmodulin-dependent protein kinase II (KN-62) did not inhibit DMPKH. DMPKH did not phosphorylate membrane-associated phosphoproteins such as acetylcholine receptor or spectrin which are known to be substrates for PKA, PKC, and CKI and -II, respectively. These experimental results suggest that the active center of the **recombinant human myotonic dystrophy** protein **kinase** may have properties distinct from the well-studied classes of serine/threonine protein kinases, in contrast to predictions based upon primary structure alone.

```
=> s "13245"
L11          44 "13245"

=> d his

     (FILE 'HOME' ENTERED AT 14:53:07 ON 03 AUG 2004)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 14:56:53 ON 03 AUG 2004
L1        14352 S MYOTONIC (A) DYSTROPHY
L2      1222659 S KINASE?
L3          999 S L1(4W)L2
L4          119 S HUMAN(A)L3
L5      6636677 S CLON? OR EXPRESS? OR RECOMBINANT
L6            0 S HUMAN(A) MDPK
L7           15 S  "MDPK"
L8          133 S L4 OR L7
L9           86 S L5 AND L8
L10          37 DUP REM L9 (49 DUPLICATES REMOVED)
L11          44 S "13245"

=> s l2 and l11
L12           3 L2 AND L11

=> dup rem l12
PROCESSING COMPLETED FOR L12
L13           2 DUP REM L12 (1 DUPLICATE REMOVED)

=> d 1-2 ibib ab

L13   ANSWER 1 OF 2  BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
      DUPLICATE 1
ACCESSION NUMBER: 2002-17868  BIOTECHDS
TITLE:            Human myotonic dystrophy type protein kinase
                  polypeptide and polynucleotide useful for prognosticating,
```

diagnosing, preventing or inhibiting tumorigenesis, tumor growth, tumor metastasis and viral infection;
vector-mediated recombinant protein gene transfer and expression in host cell for use in drug screening and gene therapy

AUTHOR: KAPELLER-LIBERMANN R
PATENT ASSIGNEE: MILLENNIUM PHARM INC
PATENT INFO: WO 2002034896 2 May 2002
APPLICATION INFO: WO 2000-US50636 23 Oct 2000
PRIORITY INFO: US 2000-242429 23 Oct 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-479720 [51]

AB DERWENT ABSTRACT:
NOVELTY - Isolated human myotonic dystrophy type protein **kinase** polypeptide (PP) (I), designated **13245**, comprising a naturally-occurring allelic variant of PP with a fully defined 2053 amino acid sequence (S1) given in the specification encoded by a nucleic acid molecule which hybridizes to a fully defined 6574 or 6159 base pair sequence (S2) given in the specification, is new.

DETAILED DESCRIPTION - Isolated human myotonic dystrophy type protein **kinase** polypeptide (PP) (I), designated **13245**, comprising a naturally-occurring allelic variant of PP with a fully defined 2053 amino acid sequence (S1) given in the specification encoded by a nucleic acid molecule which hybridizes to a fully defined 6574 or 6159 base pair sequence (S2) given in the specification. In particular (I) comprises:(i) a naturally-occurring allelic variant comprising (S1), PP encoding a nucleic acid molecule which hybridizes to (S2) or its complement under stringent conditions, (ii) a fragment comprising 15 contiguous amino acids of (S1), or (iii) a PP encoded by a nucleic acid which is at least 60% identical to (S2), or its complement. INDEPENDENT CLAIMS are also included for: (1) an isolated nucleic acid molecule (II) encoding (I) or PP comprising S1, comprising a nucleotide sequence at least 60% identical to S2 or a fragment of 300 nucleotides of S2; (2) a host cell (III) containing (II); (3) a non-human mammalian host cell containing (II); (4) an antibody (IV) that selectively binds with (I); (5) producing (I); (6) detecting (M1) the presence of (I) in a sample, by contacting the sample with a compound which selectively binds with (I) and determining whether the compound binds with (I); (7) a kit comprising a compound that selectively binds with (I) or hybridizes with (II); (8) detecting (M2) the presence of (II) in a sample, by contacting the sample with a nucleic acid probe or primer which selectively hybridizes with (II) and determining whether the nucleic acid probe or primer binds with (II); (9) modulating the activity of (I), by contacting (I) or a cell expressing (I) with a compound which binds with (I); (10) use of a modulator (V) of the activity of **13245** protein for making a medicament for modulating the ability of a cell to catalyze interconversion of the phosphorylated and de-phosphorylated forms a guanine triphosphate (GTP)ase protein; and (11) making a pharmaceutical composition for modulating e.g. interconversion of the phosphorylated and de-phosphorylated forms of a serine, threonine, or tyrosine residue of a GTPase protein, cell contractility, cell growth, cell conductivity, entry of a cell into the cell cycle, progression of a cell through the cell cycle, mitogenesis, cell metabolism, gene transcription, cytokinesis, cell shape, cell movement, integration of a viral genome into a host cell genome, maintenance of a viral genome within a host cell genome, a cytological change in a virus-infected host cell, virus production in a virus-infected host cell, interaction of a virion with a membrane of a virus-infected host cell, and encapsulation of a virion within a portion of a membrane of a virus-infected host cell, by selecting a test compound useful for modulating phenomenon and combining the test compound with a carrier.

WIDER DISCLOSURE - Disclosed are: (A) vectors containing (II); (B) chimeric or fusion proteins that includes (I) operatively linked to non-

13245 polypeptides and its use; (C) screening for compounds that modulate the expression of (II); (D) nucleic acid molecule containing a portion of S2 or complement of S2; (E) nucleic acid molecules encoding other **13245** family members having a nucleotide sequence which differ from S2; (F) nucleic acid molecules that is antisense to (II); (G) molecular beacon or detectably labeled oligonucleotide primers and probes; (H) non-human transgenic animals and its use; (I) population of cells from the above animals; (J) analyzing several capture probes or a sample; and (K) making a computer readable record of a sequence of **13245** sequence.

BIOTECHNOLOGY - Preparation: (I) is produced by culturing a mammalian host cell, under conditions in which the nucleic acid molecule is expressed. Preferred Polypeptide: (I) further comprises a heterologous amino acid sequence. Preferred Nucleic Acid: (II) further comprises a vector nucleic acid sequence, and a nucleic acid sequence encoding a heterologous PP. Preferred Method: In (M1), the compound that binds with (I) is an antibody. In (M2), the sample comprises mRNA molecules and is contacted with the nucleic acid probe. Preferred Modulator: (V) is an inhibitor of **13245** gene expression, preferably an antisense oligonucleotide comprising at least 15 nucleotide residues, which hybridizes under stringent conditions with a transcript (mRNA) of **13245** gene, or with a polynucleotide of S2. (V) does not significantly affect **13245** gene expression in the cell. (V) is an agent which inhibits an activity of 69087 protein, preferably an antibody which specifically binds with 69087 protein.

ACTIVITY - Anti-tumor; Virucide; Anti-HIV.

MECHANISM OF ACTION - Gene therapy; Modulator of (I). No supporting data is given.

USE - (I) is useful for identifying a compound which modulates the activity of (I). (I) and (III) are useful for identifying a compound which binds with (I), by determining whether (I) binds with the test compound, by direct detecting of test compound/PP binding, using a competitive binding assay or an assay for **13245**-mediated signal transduction. (I) and (III) are useful for assessing whether a test compound is useful for modulating the phenomenon such as cell contractility, cell growth, cell conductivity, and entry of a cell into the cell cycle, by adding the test compound to a first composition comprising (I) or (III), that exhibits **13245** activity, and comparing the activity in the first and second composition that is substantially identical to the first composition except that it does not comprise the test compound, where a difference in the activity indicates that the test compound is useful for modulating the phenomenon. The **13245** activity is GTPase **kinase** activity, and the composition comprises a cell comprising a nucleic acid encoding the protein, where the nucleic acid is the genome of the cell and comprises the **13245** gene. (I) and (III) are also useful for identifying a compound which is useful for modulating phenomenon (all claimed). **13245** molecules are useful as surrogate markers such as markers of disorders or disease states, as marker for precursors of disease states, as markers for predisposition of disease states, as markers for drug activity, or as markers of pharmacogenomic profile of a subject. **13245** molecules are useful to develop diagnostic and therapeutic agents for prognosticating, diagnosing, preventing, inhibiting, alleviating or curing myotonic dystrophy protein **kinase** (MDPK)-related disorders. (I) is useful to develop diagnostic and therapeutic agents for **13245**-mediated or related disorders such as tumorigenesis, tumor growth, tumor metastasis, viral infection of a cell, skeletal muscle disorders (e.g. muscular and myotonic dystrophies), immune disorders and neoplastic disorders. (I) is useful to screen for naturally occurring **13245** substrates, to screen for drugs or compounds which modulate **13245** activity, and to treat disorders characterized by insufficient or excessive production of **13245** protein or production of the protein which have decreased, aberrant or unwanted activity compared to the wild type protein. Modulator identified

by (I) is useful in treating an individual afflicted with disease or disorder characterized by aberrant or unwanted expression or activity of **13245** protein or nucleic acid molecule. (II) is useful to express a **13245** protein, to detect **13245** mRNA protein in a biological sample, to detect a genetic alteration in a **13245** gene and to modulate **13245** activity. Fragments of (II) are useful in chromosome mapping, tissue typing and aid in forensic identification of a biological sample. (I), (II) and (IV) are useful in screening assays, predictive medicine (diagnostic assays, prognostic assays, monitoring clinical trials and pharmacogenetics) and in treatment methods. (IV) is useful diagnostically to monitor **13245** protein levels in tissues and detect **13245** protein.

ADMINISTRATION - (I) is administered by parenteral (intradermal, subcutaneous, intravenous), oral, transdermal, transmucosal or rectal route or by inhalation at a dose of 0.001-30 mg/kg, preferably 0.1-20 mg/kg and (IV) at a dose of 0.1 mg/kg. Pharmaceutical composition is administered at a dose of 1 mug/kg-500 mg/kg.

EXAMPLE - Identification and characterization of human myotonic dystrophy type protein **kinase**, referred as **13245** complementary deoxyribonucleic acid (cDNA) was performed. The human **13245** nucleotide sequence which was 6574 nucleotides in length defined in the specification including non-translated regions, contains a predicted methionine-initiated coding sequence at about nucleotide residues 19-6178 and encoding a 2053 amino acid protein. (148 pages)

L13 ANSWER 2 OF 2 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-13248 BIOTECHDS
TITLE: Novel polynucleotide from coryneform bacteria coding for phosphotransferase system enzyme I, useful for isolating nucleic acids, polynucleotides or genes which code for phosphotransferase system enzyme I;
bacterium strain improvement useful for L-amino acid, especially L-lysine, production
AUTHOR: MOECKEL B; HANS S; SCHISCHKA N; PFEFFERLE W
PATENT ASSIGNEE: DEGUSSA AG
PATENT INFO: WO 2002022827 21 Mar 2002
APPLICATION INFO: WO 2000-EP10072 13 Sep 2000
PRIORITY INFO: DE 2000-1045496 13 Sep 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-383131 [41]
AB DERWENT ABSTRACT:

NOVELTY - An isolated polynucleotide (I) from coryneform bacteria comprising a sequence coding for phosphotransferase system enzyme I (ptsI) gene, such as a polynucleotide having at least 70% identity to a polynucleotide encoding a polypeptide comprising a sequence (S1) of 568 amino acids fully defined in the specification, is new.

DETAILED DESCRIPTION - (I) comprises a polynucleotide having at least 70% identity to a polynucleotide encoding a polypeptide comprising S1, a polynucleotide coding for a polypeptide comprising a sequence having at least 70% identity to S1, a polynucleotide complementary to the above mentioned polynucleotides, or a polynucleotide comprising at least 15 successive nucleotides of the above mentioned polynucleotides, where the polypeptide preferably has the activity of ptsI. INDEPENDENT CLAIMS are also included for the following (1) a coryneform bacterium (II) in which the ptsI gene is enhanced, preferably over-expressed; (2) Corynebacterium glutamicum DSM5715/pEC-K18mob2 deposited as DSM **13245** at the Deutsche Sammlung fur Mikroorganismen and Zellkulturen (German collection of Microorganisms and Cell Cultures), DSMZ, Braunschweig, Germany; (3) Escherichia coli strain DH5alphamcr/pEC-K18mob2ptsIexp (=DH5alphamcr/pEC-K18mob2ptsIexp) deposited as DSM 14278 at the Deutsche Sammlung fur Mikroorganismen und Zellkulturen (German collection of Microorganisms and Cell Cultures), DSMZ, Braunschweig, Germany; (4) a process for the preparation of L-amino

acids; (5) a DNA (III) which originates from coryneform bacteria and codes for ptsI, where the associated amino acid sequences between positions 120-127 and/or 134-140 in S1 are altered by amino acid exchange, the associated amino acid sequences at position 123 in S1 contain any other proteinogenic amino acid excluding L-lysine, preferably L-glutamic acid or L-aspartic acid, the associated amino acid sequences at position 137 in S1 contain any other proteinogenic amino acid excluding L-arginine, preferably L-cysteine, or the associated amino acid sequences at position 123 contains glutamic acid and at position 137 contains L-cysteine; and (6) a coryneform bacterium which contains (III) or a vector which carries (I).

WIDER DISCLOSURE - Also disclosed are (1) a vector containing (I); and (2) a polynucleotide consisting substantially of a polynucleotide sequence, that is obtainable by screening by hybridizing a corresponding gene library of a coryneform bacterium, which comprises the complete gene or its part, with a probe which comprises the polynucleotide sequence (S2) comprising 2005 nucleotides fully defined in the specification, or its fragment, and isolating the DNA sequence.

BIOTECHNOLOGY - Preferred Sequence: (I) is preferably a recombinant DNA replicable in coryneform bacteria, or a RNA. (I) is capable of replication and comprises a sequence (S2) of 2005 nucleotides fully defined in the specification, at least one sequence that corresponds to S2 within the range of degeneration of the genetic code, at least one sequence that hybridizes with the sequences complementary to the above mentioned sequences, and optionally sense mutations of neutral function in S2. (III) contains the nucleobase guanine at position 520 and thymine at position 562 in S2. Preparation: (II) is useful for fermentative preparation of L-amino acids, such as L-lysine, by fermenting (II) which produces the desired L-amino acid and in which the ptsI gene or nucleotide sequences which encode for it are enhanced, concentrating the L-amino acid in the medium or in the cells of the bacteria, and isolating the L-amino acid. The method employs bacteria in which further genes of the biosynthesis pathway of the desired L-amino acid are additionally enhanced, bacteria in which metabolic pathways which reduce the formation of the desired L-amino acid are at least partly eliminated, and a strain transformed with a plasmid vector which carries the sequence coding for the ptsI gene. The expression of the polynucleotide(s) which code(s) for the ptsI gene is enhanced, preferably over-expressed. The catalytic properties of the polypeptide (enzyme protein) for which the polynucleotide ptsI codes are increased. For the preparation of L-amino acids, coryneform microorganisms in which at the same time one or more genes chosen from the dapA gene which codes for dihydrodipicolinate synthase, the gap gene which codes for glyceraldehyde 3-phosphate dehydrogenase, the tpi gene which codes for triose phosphate isomerase, the pgk gene which codes for 3-phosphoglycerate **kinase**, the zwf gene which codes for glucose 6-phosphate dehydrogenase, the pyc gene which codes for pyruvate carboxylase, the mqo gene which codes for malate-quinone oxidoreductase, the lysC gene which codes for a feed-back resistant aspartate **kinase**, the lysE gene which codes for lysine export, the hom gene which codes for homoserine dehydrogenase, the ilvA gene which codes for threonine dehydratase or the ilvA (Fbr) allele which codes for a feed back resistant threonine dehydratase, the ilvBN gene which codes for acetohydroxy acid synthase, the ilvD gene which codes for dihydroxy-acid dehydratase, and the zwa1 gene which codes for the zwa1 protein is or are enhanced or over-expressed are fermented. For the preparation of L-amino acids, coryneform microorganisms in which at the same time one or more genes chosen from the pck gene which codes for pyruvate carboxykinase, the pgi gene which codes for glucose 6-phosphate isomerase, the poxB gene which codes for pyruvate oxidase, the zwa2 gene which codes for zwa2 protein, is or are attenuated are fermented.

USE - (I) is useful for discovering RNA, cDNA and DNA in order to isolate nucleic acids, or polynucleotides or genes which code for ptsI or have a high similarity with the sequence of the ptsI, where the method involves use of arrays, microarrays, or DNA chips. The microorganisms of

the species C.glutamicum, preferably C.glutamicum strain DSM5715/pEC-K18mob2 or DH5alphamcr/pEC-K18mob2ptsIexp is employed in the above mentioned method (claimed). (I) is also useful as a primer.

EXAMPLE - A genomic cosmid gene library from Corynebacterium glutamicum ATCC 13032 was produced. Isolation and sequencing of the phosphotransferase system enzyme I (ptsI) gene, was as follows. The cosmid DNA of an individual colony was isolated and was partially cleaved with the restriction enzyme Sau3AI. The DNA fragments were dephosphorylated with shrimp alkaline phosphatase. After separation by gel electrophoresis, cosmid fragments of the order of 1500-2000 base pairs were isolated. The DNA of the sequencing vector pZero-1 was cleaved with the restriction enzyme BamHI. Ligation of the cosmid fragments in the sequencing vector pZero-1 was effected and the DNA mixture was incubated overnight with T4 ligase. This ligation mix was electroporated into the Escherichia colistrain DH5alphaMCR and the batch was plated out on LB agar with 50 mg/l zeocin. The plasmid was prepared from the recombinant clone and sequencing was performed. The nucleotide sequence obtained had 2005 base pairs fully defined in the specification and encoded a protein comprising 568 amino acids fully defined in the specification. (56 pages)

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     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 14:56:53 ON 03 AUG 2004
L1         14352 S MYOTONIC (A) DYSTROPHY
L2       1222659 S KINASE?
L3           999 S L1(4W)L2
L4           119 S HUMAN(A)L3
L5       6636677 S CLON? OR EXPRESS? OR RECOMBINANT
L6             0 S HUMAN(A) MDPK
L7            15 S  "MDPK"
L8           133 S L4 OR L7
L9            86 S L5 AND L8
L10           37 DUP REM L9 (49 DUPLICATES REMOVED)
L11           44 S "13245"
L12            3 S L2 AND L11
L13            2 DUP REM L12 (1 DUPLICATE REMOVED)

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E1             3     KAPELLER SHE A M/AU
E2             1     KAPELLER W/AU
E3             0 --> KAPELLER-LIBERMANN R/AU
E4             1     KAPELLERADLER REGINE/AU
E5             1     KAPELLERLIBERMAN R/AU
E6             1     KAPELLEROV A A/AU
E7           103     KAPELLEROVA A/AU
E8             2     KAPELLEROVA ALICA/AU
E9             2     KAPELLEROVA O/AU
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E12            1     KAPELLI O/AU

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E12           1      KAPELLERADLER REGINE/AU

=> e kapellerlibermann r/au
E1            1      KAPELLERADLER REGINE/AU
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E3            0 --> KAPELLERLIBERMANN R/AU
E4            1      KAPELLEROV A A/AU
E5          103      KAPELLEROVA A/AU
E6            2      KAPELLEROVA ALICA/AU
E7            2      KAPELLEROVA O/AU
E8            1      KAPELLEVICH S L/AU
E9            1      KAPELLI J P/AU
E10           1      KAPELLI O/AU
E11           1      KAPELLI S/AU
E12           1      KAPELLIER LIBERMANN R/AU

=> e kapeller(w)libermann r/au
E1            3      KAPELLER SHE A M/AU
E2            1      KAPELLER W/AU
E3            0 --> KAPELLER(W)LIBERMANN R/AU
E4            1      KAPELLERADLER REGINE/AU
E5            1      KAPELLERLIBERMAN R/AU
E6            1      KAPELLEROV A A/AU
E7          103      KAPELLEROVA A/AU
E8            2      KAPELLEROVA ALICA/AU
E9            2      KAPELLEROVA O/AU
E10           1      KAPELLEVICH S L/AU
E11           1      KAPELLI J P/AU
E12           1      KAPELLI O/AU

=> e kapellerl r/au
E1            1      KAPELLER W/AU
E2            1      KAPELLERADLER REGINE/AU
E3            0 --> KAPELLERL R/AU
E4            1      KAPELLERLIBERMAN R/AU
E5            1      KAPELLEROV A A/AU
E6          103      KAPELLEROVA A/AU
E7            2      KAPELLEROVA ALICA/AU
E8            2      KAPELLEROVA O/AU
E9            1      KAPELLEVICH S L/AU
E10           1      KAPELLI J P/AU
E11           1      KAPELLI O/AU
E12           1      KAPELLI S/AU

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=> s e5-e10
L14         191 ("KAPELLER LIBERMAN ROSANA"/AU OR "KAPELLER LIBERMANN R"/AU OR
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                U OR "KAPELLER LIEBERMANN R"/AU OR "KAPELLER LIEBERMANN ROSANA"/
                AU)

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     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 14:56:53 ON 03 AUG 2004
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L7            15 S  "MDPK"
L8           133 S L4 OR L7
L9            86 S L5 AND L8
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L12            3 S L2 AND L11
L13            2 DUP REM L12 (1 DUPLICATE REMOVED)
                 E KAPELLER-LIBERMANN R/AU
                 E KAPELLER R/AU
                 E KAPELLERLIBERMANN R/AU
                 E KAPELLER(W)LIBERMANN R/AU
                 E KAPELLERL R/AU
                 E KAPELLER L R/AU
L14          191 S E5-E10

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L15            2 L8 AND L14

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L15   ANSWER 1 OF 2  BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-17868  BIOTECHDS
TITLE:            Human myotonic dystrophy type
                  protein kinase polypeptide and polynucleotide
                  useful for prognosticating, diagnosing, preventing or
                  inhibiting tumorigenesis, tumor growth, tumor metastasis and
                  viral infection;
                     vector-mediated recombinant protein gene transfer and
                     expression in host cell for use in drug screening and gene
                     therapy
AUTHOR:           KAPELLER-LIBERMANN R
PATENT ASSIGNEE:  MILLENNIUM PHARM INC
PATENT INFO:      WO 2002034896 2 May 2002
APPLICATION INFO: WO 2000-US50636 23 Oct 2000
PRIORITY INFO:    US 2000-242429 23 Oct 2000
DOCUMENT TYPE:    Patent
LANGUAGE:         English
OTHER SOURCE:     WPI: 2002-479720 [51]
AB    DERWENT ABSTRACT:
      NOVELTY - Isolated human myotonic dystrophy
      type protein kinase polypeptide (PP) (I), designated 13245,
      comprising a naturally-occurring allelic variant of PP with a fully
      defined 2053 amino acid sequence (S1) given in the specification encoded
      by a nucleic acid molecule which hybridizes to a fully defined 6574 or
      6159 base pair sequence (S2) given in the specification, is new.
           DETAILED DESCRIPTION - Isolated human myotonic
      dystrophy type protein kinase polypeptide (PP) (I),
      designated 13245, comprising a naturally-occurring allelic variant of PP
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with a fully defined 2053 amino acid sequence (S1) given in the specification encoded by a nucleic acid molecule which hybridizes to a fully defined 6574 or 6159 base pair sequence (S2) given in the specification. In particular (I) comprises:(i) a naturally-occurring allelic variant comprising (S1), PP encoding a nucleic acid molecule which hybridizes to (S2) or its complement under stringent conditions, (ii) a fragment comprising 15 contiguous amino acids of (S1), or (iii) a PP encoded by a nucleic acid which is at least 60% identical to (S2), or its complement. INDEPENDENT CLAIMS are also included for: (1) an isolated nucleic acid molecule (II) encoding (I) or PP comprising S1, comprising a nucleotide sequence at least 60% identical to S2 or a fragment of 300 nucleotides of S2; (2) a host cell (III) containing (II); (3) a non-human mammalian host cell containing (II); (4) an antibody (IV) that selectively binds with (I); (5) producing (I); (6) detecting (M1) the presence of (I) in a sample, by contacting the sample with a compound which selectively binds with (I) and determining whether the compound binds with (I); (7) a kit comprising a compound that selectively binds with (I) or hybridizes with (II); (8) detecting (M2) the presence of (II) in a sample, by contacting the sample with a nucleic acid probe or primer which selectively hybridizes with (II) and determining whether the nucleic acid probe or primer binds with (II); (9) modulating the activity of (I), by contacting (I) or a cell expressing (I) with a compound which binds with (I); (10) use of a modulator (V) of the activity of 13245 protein for making a medicament for modulating the ability of a cell to catalyze interconversion of the phosphorylated and de-phosphorylated forms a guanine triphosphate (GTP)ase protein; and (11) making a pharmaceutical composition for modulating e.g. interconversion of the phosphorylated and de-phosphorylated forms of a serine, threonine, or tyrosine residue of a GTPase protein, cell contractility, cell growth, cell conductivity, entry of a cell into the cell cycle, progression of a cell through the cell cycle, mitogenesis, cell metabolism, gene transcription, cytokinesis, cell shape, cell movement, integration of a viral genome into a host cell genome, maintenance of a viral genome within a host cell genome, a cytological change in a virus-infected host cell, virus production in a virus-infected host cell, interaction of a virion with a membrane of a virus-infected host cell, and encapsulation of a virion within a portion of a membrane of a virus-infected host cell, by selecting a test compound useful for modulating phenomenon and combining the test compound with a carrier.

WIDER DISCLOSURE - Disclosed are: (A) vectors containing (II); (B) chimeric or fusion proteins that includes (I) operatively linked to non-13245 polypeptides and its use; (C) screening for compounds that modulate the expression of (II); (D) nucleic acid molecule containing a portion of S2 or complement of S2; (E) nucleic acid molecules encoding other 13245 family members having a nucleotide sequence which differ from S2; (F) nucleic acid molecules that is antisense to (II); (G) molecular beacon or detectably labeled oligonucleotide primers and probes; (H) non-human transgenic animals and its use; (I) population of cells from the above animals; (J) analyzing several capture probes or a sample; and (K) making a computer readable record of a sequence of 13245 sequence.

BIOTECHNOLOGY - Preparation: (I) is produced by culturing a mammalian host cell, under conditions in which the nucleic acid molecule is expressed. Preferred Polypeptide: (I) further comprises a heterologous amino acid sequence. Preferred Nucleic Acid: (II) further comprises a vector nucleic acid sequence, and a nucleic acid sequence encoding a heterologous PP. Preferred Method: In (M1), the compound that binds with (I) is an antibody. In (M2), the sample comprises mRNA molecules and is contacted with the nucleic acid probe. Preferred Modulator: (V) is an inhibitor of 13245 gene expression, preferably an antisense oligonucleotide comprising at least 15 nucleotide residues, which hybridizes under stringent conditions with a transcript (mRNA) of 13245 gene, or with a polynucleotide of S2. (V) does not significantly affect 13245 gene expression in the cell. (V) is an agent which inhibits an activity of 69087 protein, preferably an antibody which specifically

binds with 69087 protein.

ACTIVITY - Anti-tumor; Virucide; Anti-HIV.

MECHANISM OF ACTION - Gene therapy; Modulator of (I). No supporting data is given.

USE - (I) is useful for identifying a compound which modulates the activity of (I). (I) and (III) are useful for identifying a compound which binds with (I), by determining whether (I) binds with the test compound, by direct detecting of test compound/PP binding, using a competitive binding assay or an assay for 13245-mediated signal transduction. (I) and (III) are useful for assessing whether a test compound is useful for modulating the phenomenon such as cell contractility, cell growth, cell conductivity, and entry of a cell into the cell cycle, by adding the test compound to a first composition comprising (I) or (III), that exhibits 13245 activity, and comparing the activity in the first and second composition that is substantially identical to the first composition except that it does not comprise the test compound, where a difference in the activity indicates that the test compound is useful for modulating the phenomenon. The 13245 activity is GTPase kinase activity, and the composition comprises a cell comprising a nucleic acid encoding the protein, where the nucleic acid is the genome of the cell and comprises the 13245 gene. (I) and (III) are also useful for identifying a compound which is useful for modulating phenomenon (all claimed). 13245 molecules are useful as surrogate markers such as markers of disorders or disease states, as marker for precursors of disease states, as markers for predisposition of disease states, as markers for drug activity, or as markers of pharmacogenomic profile of a subject. 13245 molecules are useful to develop diagnostic and therapeutic agents for prognosticating, diagnosing, preventing, inhibiting, alleviating or curing myotonic dystrophy protein kinase (**MDPK**)-related disorders. (I) is useful to develop diagnostic and therapeutic agents for 13245-mediated or related disorders such as tumorigenesis, tumor growth, tumor metastasis, viral infection of a cell, skeletal muscle disorders (e.g. muscular and myotonic dystrophies), immune disorders and neoplastic disorders. (I) is useful to screen for naturally occurring 13245 substrates, to screen for drugs or compounds which modulate 13245 activity, and to treat disorders characterized by insufficient or excessive production of 13245 protein or production of the protein which have decreased, aberrant or unwanted activity compared to the wild type protein. Modulator identified by (I) is useful in treating an individual afflicted with disease or disorder characterized by aberrant or unwanted expression or activity of 13245 protein or nucleic acid molecule. (II) is useful to express a 13245 protein, to detect 13245 mRNA protein in a biological sample, to detect a genetic alteration in a 13245 gene and to modulate 13245 activity. Fragments of (II) are useful in chromosome mapping, tissue typing and aid in forensic identification of a biological sample. (I), (II) and (IV) are useful in screening assays, predictive medicine (diagnostic assays, prognostic assays, monitoring clinical trials and pharmacogenetics) and in treatment methods. (IV) is useful diagnostically to monitor 13245 protein levels in tissues and detect 13245 protein.

ADMINISTRATION - (I) is administered by parenteral (intradermal, subcutaneous, intravenous), oral, transdermal, transmucosal or rectal route or by inhalation at a dose of 0.001-30 mg/kg, preferably 0.1-20 mg/kg and (IV) at a dose of 0.1 mg/kg. Pharmaceutical composition is administered at a dose of 1 mug/kg-500 mg/kg.

EXAMPLE - Identification and characterization of **human myotonic dystrophy** type protein **kinase**, referred as 13245 complementary deoxyribonucleic acid (cDNA) was performed. The human 13245 nucleotide sequence which was 6574 nucleotides in length defined in the specification including non-translated regions, contains a predicted methionine-initiated coding sequence at about nucleotide residues 19-6178 and encoding a 2053 amino acid protein. (148 pages)

L15 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:332324 HCAPLUS
DOCUMENT NUMBER: 136:351429
TITLE: Protein and cDNA sequences of a novel **human myotonic dystrophy** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof
INVENTOR(S): **Kapeller-Libermann, Rosana**
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002034896	A2	20020502	WO 2001-US50636	20011023
WO 2002034896	A3	20021024		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002034132	A5	20020506	AU 2002-34132	20011023
US 2002160483	A1	20021031	US 2001-17216	20011023
EP 1328621	A2	20030723	EP 2001-985157	20011023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-242429P P 20001023
WO 2001-US50636 W 20011023

AB The invention provides protein and cDNA sequences of a novel human protein, designated 13245, which has sequence homol. with myotonic dystrophy protein kinase. The invention also provides antisense nucleic acid mols., recombinant expression vectors containing 13245 nucleic acid mols., host cells into which the expression vectors have been introduced, and non-human transgenic animals in which a 13245 gene has been introduced or disrupted. The invention still further provides isolated 13245 proteins, fusion proteins, antigenic peptides and anti-13245 antibodies. Diagnostic methods utilizing compns. of the invention are also provided.

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(FILE 'HOME' ENTERED AT 14:53:07 ON 03 AUG 2004)

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L7	15	S "MDPK"
L8	133	S L4 OR L7
L9	86	S L5 AND L8
L10	37	DUP REM L9 (49 DUPLICATES REMOVED)
L11	44	S "13245"

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L12           3 S L2 AND L11
L13           2 DUP REM L12 (1 DUPLICATE REMOVED)
                E KAPELLER-LIBERMANN R/AU
                E KAPELLER R/AU
                E KAPELLERLIBERMANN R/AU
                E KAPELLER(W)LIBERMANN R/AU
                E KAPELLERL R/AU
                E KAPELLER L R/AU
L14         191 S E5-E10
L15           2 S L8 AND L14
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	Issue Date	Pages	Document ID	Title
1	20040624	106	US 20040121383 A1	Compositions, organisms and methodologies employing a novel human kinase
2	20040610	22	US 20040110177 A1	Method for identifying functional nucleic acids
3	20040513	207	US 20040091993 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
4	20040415	64	US 20040072184 A1	Cancer associated protein kinases and their uses
5	20040408	47	US 20040068380 A1	Human gtp-rho binding protein 2
6	20040325	117	US 20040059519 A1	Multiplexed analysis of clinical specimens apparatus and methods
7	20040325	135	US 20040058340 A1	Diagnosis and prognosis of breast cancer patients
8	20040226	259	US 20040038207 A1	Gene expression in bladder tumors
9	20040129	84	US 20040018522 A1	Identification of dysregulated genes in patients with multiple sclerosis
10	20040115	49	US 20040009502 A1	Identification and tissue distribution of two novel spliced variants of the mouse LATS2 gene
11	20040101	24	US 20040003424 A1	Transgenic cardiomyocytes with controlled proliferation and differentiation

	Issue Date	Pages	Document ID	Title
12	20031113	136	US 20030211093 A1	Human kinases
13	20030313	81	US 20030049795 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
14	20030306	202	US 20030044783 A1	Human genes and gene expression products
15	20030220	297	US 20030036505 A1	Signal transduction pathway component polynucleotides, polypeptides, antibodies and methods based thereon
16	20030130	207	US 20030022340 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
17	20021114	345	US 20020168711 A1	Nucleic acids, proteins, and antibodies
18	20021031	89	US 20020160483 A1	13245, a novel human myotonic dystrophy type protein kinase and uses therefor
19	20020919	184	US 20020132322 A1	ISOLATED HUMAN KINASE PROTEINS, NUCLEIC ACID MOLECULES ENCODING HUMAN KINASE PROTEINS, AND USES THEREOF

	Issue Date	Pages	Document ID	Title
20	20020919		US 20020132247 A1	Dystrophia myotonica protein kinase (DM-PK) and its uses
21	20020905		US 20020123474 A1	Human GTP-Rho binding protein2
22	20020530		US 20020065394 A1	Secreted proteins and polynucleotides encoding them
23	20020523		US 20020061571 A1	Novel isoform of myotonic dystrophy associated protein kinase and uses thereof
24	20040217		US 6692948 B2	Isolated human kinase proteins
25	20040120		US 6680188 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
26	20031028	78	US 6638745 B1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
27	20021112	202	US 6479269 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
28	20020910		US 6449562 B1	Multiplexed analysis of clinical specimens apparatus and method
29	20020101	227	US 6335170 B1	Gene expression in bladder tumors

	Issue Date	Pages	Document ID	Title
30	20010710		US 6258776 B1	Calcium-regulated kinase
31	20000502		US 6057107 A	Methods and compositions for flow cytometric determination of DNA sequences
32	19980407		US 5736330 A	Method and compositions for flow cytometric determination of DNA sequences

	Issue Date	Pages	Document ID	Title
1	20040624	106	US 20040121383 A1	Compositions, organisms and methodologies employing a novel human kinase
2	20040513	207	US 20040091993 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
3	20040415	64	US 20040072184 A1	Cancer associated protein kinases and their uses
4	20040226	259	US 20040038207 A1	Gene expression in bladder tumors
5	20040115	49	US 20040009502 A1	Identification and tissue distribution of two novel spliced variants of the mouse LATS2 gene
6	20030313	81	US 20030049795 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
7	20030306	202	US 20030044783 A1	Human genes and gene expression products
8	20030130	207	US 20030022340 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
9	20021031	89	US 20020160483 A1	13245, a novel human myotonic dystrophy type protein kinase and uses therefor

	Issue Date	Pages	Document ID	Title
10	20020919	184	US 20020132322 A1	ISOLATED HUMAN KINASE PROTEINS, NUCLEIC ACID MOLECULES ENCODING HUMAN KINASE PROTEINS, AND USES THEREOF
11	20020919	21	US 20020132247 A1	Dystrophia myotonica protein kinase (DM-PK) and its uses
12	20020530	284	US 20020065394 A1	Secreted proteins and polynucleotides encoding them
13	20020523	26	US 20020061571 A1	Novel isoform of myotonic dystrophy associated protein kinase and uses thereof
14	20040217	66	US 6692948 B2	Isolated human kinase proteins
15	20040120	202	US 6680188 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
16	20031028	78	US 6638745 B1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
17	20021112	202	US 6479269 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
18	20020101	227	US 6335170 B1	Gene expression in bladder tumors

	Issue Date	Pages	Document ID	Title
19	20010710	22	US 6258776 B1	Calcium-regulated kinase

	Issue Date	Pages	Document ID	Title
1	20040729	117	US 20040147718 A1	Nucleotide and protein sequences of lats genes and methods based thereon
2	20040311	74	US 20040048816 A1	Restenosis treatment
3	20040212	87	US 20040029124 A1	Mrna amplification
4	20031127	50	US 20030219716 A1	Method and apparatus for improving in vitro measurement of membrane permeability of chemical compounds
5	20021031	89	US 20020160483 A1	13245, a novel human myotonic dystrophy type protein kinase and uses therefor
6	20020815	170	US 20020110811 A1	Variants of protein kinases
7	20031007	112	US 6630613 B1	Transgenic animals and lats genes
8	20030506	112	US 6559285 B1	Nucleotide and protein sequences of lats genes and methods based thereon
9	20020319	112	US 6359193 B1	Nucleotide sequences of lats genes
10	19991130	116	US 5994503 A	Nucleotide and protein sequences of lats genes and methods based thereon

	Issue Date	Pages	Document ID	Title
1	20021031	89	US 20020160483 A1	13245, a novel human myotonic dystrophy type protein kinase and uses therefor

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1	20021031	89	US 20020160483 A1	13245, a novel human myotonic dystrophy type protein kinase and uses therefor

	L #	Hits	Search Text
1	L1	834	myotonic adj dystrophy
2	L2	50060	kinase$2
3	L3	73	l1 adj5 l2
4	L4	647231	clon$3 or express$3 or recombinant
5	L5	32	l3 same l4
6	L6	425481	human
7	L7	19	l5 same l6
8	L8	10	"MDPK"
9	L9	170	"13245"
10	L10	1	l3 same l9
11	L11	190	KAPELLER
12	L12	77	l3 or l8
13	L13	1	l11 and l12